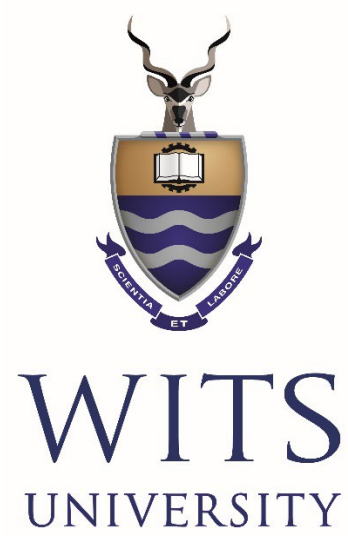
MALARIA RELATED KNOWLEDGE AND PREVENTION PRACTICES: A COMPARATIVE STUDY BETWEEN SOUTH AFRICA AND NIGERIA; AND EFFICACY OF COMMERCIALLY-AVAILABLE MOSQUITO REPELLANTS

Mustapha Aliero Halidu



A Dissertation submitted to the Division of Pharmacology, Department of Pharmacy and Pharmacology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree

of

Master of Science in Medicine.

Johannesburg 2022

DECLARATION

I, Halidu Aliero Mustapha declare that the work on which this dissertation is based is my original work. All the contributions made by other people to this dissertation have been duly acknowledged. It is being submitted for the degree of Master of Medicine (Clinical and experimental Pharmacology) at the University of the Witwatersrand, Johannesburg, South Africa. This work has not been submitted before for any degree or examination at this or any other university.

……

Mustapha Aliero Halidu (1966648)

DEDICATION

I dedicate this work to my loving parents: Alhaji Halidu Abdullahi Aliero and Hajiya Fatima Sarkin Yaki Aliero; my wife Suwaiba Abubakar Aliero; my uncle Haruna Sa'adu Aliero and my kids for their prayers and support throughout the course of this work.

CONFERRENCE PROCEEDINGS

MH Aliero, R van Zyl, S Schmollgruber, L Koekemoer. Knowledge of Health Care Professionals on Management of Malaria in Johannesburg, South Africa. Faculty of Health Sciences Research Day, WITS University, South Africa. 15 October 2020 [Oral]

MH Aliero, RL van Zyl, S Schmollgruber, L Koekemoer. Market and Online Survey, and Efficacy of fifteen commercially available mosquito repellents in Johannesburg, South Africa. Keystone eSymposia - Malaria in the Era of COVID-19, Virtual Conference, 6-7 March 2021. [poster presentation]

MH Aliero, LL Koekemoer, S Schmollgruber, RL van Zyl. Knowledge, Attitudes and Perception of University of Witwatersrand Faculty of Health Sciences Students on Malaria Management and Prevention. 6th Annual Southern Africa Malaria Research Conference, Research & Control: United Against Malaria, 3 & 4 August 2021, Virtual Event. [poster presentation]

MH Aliero, S. Schmollgruber, LL Koekemoer, RL van Zyl. Market - Online Survey and Efficacy of Fifteen Commercially Available Mosquito Repellents in Johannesburg, South Africa. 12th Cross-Faculty Postgraduate Symposium, Online, 26-28, 30th July 2021 [poster presentation]

MH Aliero, LL Koekemoer, S Schmollgruber, RL van Zyl. Knowledge, Attitudes and Perception of University of the Witwatersrand Faculty of Health Sciences Students on Malaria Management and Prevention. School of Therapeutic Sciences Research Day, WITS University, 14 September 2021. Online. [poster].

MH Aliero, R van Zyl, S Schmollgruber, L Koekemoer. Knowledge of Health Care Professionals on Management of Malaria in Johannesburg, South Africa. Faculty of Health Sciences Research Day, WITS University, 2020, South Africa. [Oral].

MH Aliero, RL van Zyl, S Schmollgruber, L Koekemoer. Market and Online Survey, and Efficacy of fifteen commercially available mosquito repellents in Johannesburg, South Africa. Keystone eSymposia - Malaria in the Era of COVID-19, Virtual Conference, 6-7 March 2021. [Scitalk oral presentation].

Robyn L van Zyl, **Mustapha H Aliero**, Obaidiyah Mustapha, Babita Canga, Lizette L. Koekemoer. The spectrum of activity of citronella in the prevention and eradication of malaria. 4th International Congress on Parasites of Wildlife (ICPOW)- Parasitological Society of Southern Africa (PARSA) . Skukuza, South Africa, during 11-15 September 2022**.**

ABSTRACT

Plasmodium parasites cause serious, but treatable febrile illness if managed early with effective therapies. Malaria infections have been linked to various factors like vector dynamics, environmental changes and individual or community factors such as malaria knowledge and practice behaviours. This study compared these latter two factors between South African and Nigerian healthcare professionals and communities. As well as assessed the efficacy of fifteen commercially available mosquito repellents reportedly used and available in Johannesburg South Africa.

The cross-sectional survey on the knowledge, attitudes, and practices of respondents on malaria management was conducted with a semi-structured questionnaire. A total of 1,144 questionnaires were completed by 752 South Africans (65.7%) and 392 Nigerians (34.3%). Most respondents had good malaria-related knowledge (68.8%; n = 779), with a significantly higher ($p < 0.001$) proportion from South Africa (73.8%) compared to Nigeria (59.2%). The malaria-related knowledge was found to be associated with the respondent's gender ($p=0.022$), educational status ($p<0.034$), occupational status (<0.001) and age ($p<0.001$). More misconception on the malaria vector was seen among the South African respondents. The healthcare professionals (HCPs) knowledge of first line therapies for management of both uncomplicated and severe malaria was significantly different ($p<0.001$) between the study countries. In general, a total of 82.1% of the participants have used mosquito repellents with 84.5% in Nigeria compared to 80.8% South Africans.

After collating information on commercially available repellents, the efficacy of 15 commercial repellents were compared to DEET in a non-contact test chamber housing starved female *Anopheles gambiae* mosquitoes. The DEET (Tabard™ lotion; 19.5%) provided a mean protection of 99.1 ± 0.87% for all four tested volunteers; with a slightly higher mean protection of 99.45 ± 0.3% obtained with Medi-scabiol™ soap (citronella oil). Of the recorded repellents, only 59.8% specified SABS approval on the product.

In conclusion, despite the good knowledge and attitude of the respondents, there were some misconceptions amongst the respondents from both countries that could be improved through continuing education. Furthermore, the citronella-based repellent products are effective for short-term personal protection from mosquito bites, however, DEET remains the gold standard repellent product for long-term protection. Consumers are advised to check for SABS approval for any product they intend to use to ensure optimal protection.

ACKNOWLEDGEMENT

Firstly, I thank the Almighty Allah for keeping me healthy and making me resilient throughout the course of this programme.

I am extremely grateful to my supervisors: Professor Robyn van Zyl, Professor Shelley Schmollgruber and Professor Lizette Koekemoer who have demonstrated a great support, commitment, and mentorship throughout the programme. Surely you taught me to be patience, hardworking, and committed to my work.

My sincere gratitude goes to Dr Innocent Maposa who was responding to the series of my emails during data analysis and Amanda Calitz who guided me on how to use the REDCap during questionnaire design.

I am grateful to Thando Radebe who was always around during the repellent efficacy assays and assisted in setting up the instruments and provided any technical support that may be needed.

I am grateful to the Division of Pharmacology, Department of Pharmacy and Pharmacology for the opportunities giving to me to attend courses and conferences.

I would like to acknowledge the contributions of WRIM research colleagues especially Mbuyi Kalonji who was always there for me during repellent efficacy assays.

I extremely appreciate the financial support from the Tertiary Education Trust Fund (TETFUND), Nigeria and Faculty of Health Sciences Research Office, University of the Witwatersrand, South Africa.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABREVIATIONS

ACT:	Artemisinin-based Combination Therapy
AIDS:	Acquired Immunodeficiency Syndrome
AST:	Aspartate amino Transferase
CDC:	Centre for Disease and Control
CHBAH:	Chris-Hani Baragwanath Academic Hospital
CHS:	College of Health Sciences
CI:	Confidence Interval
CMJAH:	Charlotte Maxeke Johannesburg Academic Hospital
CYP450:	Cytochrome P450 enzymes
DDT:	Dichlorodiphenyltrichloroethane
DEET:	N, N-Diethyl-3-meta-Toluamide
DEPA:	N, N-Diethyl-2-Phenyl-Acetamide
DHFR:	Dihydrofolate reductase enzyme
ECG:	Echocardiography
FHS:	Faculty of Health Sciences
FMC:	Federal Medical Centre
FMOH:	Federal Ministry of Health
FUBK:	Federal University Birnin Kebbi
HIV:	Human Immunodeficiency Virus
HCPs:	Healthcare Professionals
HRP2:	Histidine Reach Protein 2
HSD:	Honestly Significant Difference Test
IQR:	Inter Quartile Range
IR3535:	Insect Repellent 3535
IRS:	Indoor Residual Spray
ITN:	Insecticide Treated Net
LAMP:	Loop Mediated Isothermal Amplification
LDH:	Lactate Dehydrogenase
LGBTI:	Lesbian, Transgender, Bisexual, Transgender, and Intersex
LLINs:	Long Lasting Insecticide Treated Nets
MDGs:	Millennium Development Goals
NCAC:	Number of mosquitoes in the Control Arm Chamber
NG:	Nigeria

NTAC:	Number of mosquitoes in the Treated Arm Chamber
OR:	Odd Ratio
PCR:	Polymerase Chain Reaction
PMD:	Para-Menthane-3-8-Diol
QBC:	Quantitative Buffy Coat Method
QT-NASBA:	Quantitative Nucleic Acid Sequence-Based Amplification
RBCs:	Red Blood Cells
RBM:	Roll Back Malaria
RDT:	Rapid Diagnostic Test
REDCap:	Research Electronic Data Capture
RT-PCR:	Reverse Transcription Polymerase Chain Reaction
SA:	South Africa
SABS:	South African Bureau of Standards
SADOH:	South African Department of Health
SAHPRA:	South African Health Products Regulatory Authority
SAI:	Spatial Activity Index
SANAS	South African National Accreditations System
S.D	Standard deviation
SDG:	Sustainable Development Goals
SOP:	Standard Operations Procedure
SYMH:	Sir Yahya Memorial Hospital
UMT:	Urine Malaria Test
V1- V4:	Volunteer One to Volunteer Four
WHO:	World Health Organisation
WRIM:	WITS Research Institute for Malaria

CHAPTER ONE:
INTRODUCTION AND LITERATURE REVIEW

1.1 Malaria and Epidemiology

Malaria the disease as old as humanity itself, is often called the “king of diseases” because it has killed mankind in the history more than any other disease or war (MalariaSite, 2016). The cause of this deadly disease is an apicomplexan parasite in the genus *Plasmodium* that infects many vertebrates, causing a serious, but treatable febrile illness if early and effective therapies are instituted (Gilson et al., 2019). The genus *Plasmodium* has 156 species, however only five of these commonly cause disease in humans, which include: *Plasmodium falciparum, P. vivax, P. ovalae, P. malariae* and *P. knowlesi* (Aguiar et al., 2019).

The *P. knowlesi,* previously considered to cause zoonotic malaria in old world monkeys is now reported to cause malaria in humans. *P. knowlesi* infections are commonly misdiagnosed as *P. malariae* (Singh et al., 2004; Raja et al., 2020). Recently Karunajeewa and Berman (2019) reported a spike of human malaria cases caused by *P. knowlesi* in Sabah, Malaysia. Although mainly reported from Asia, infections with *P. knowlesi* are often severe and fatal, hence attracting global attention (Cox-Singh et al., 2008; Raja et al., 2020).

The other zoonotic species reported in Brazil to cause malaria in humans includes *P. simium* (Brasil et al., 2017), *P. cyanomolgi* identified from Malaysia (Ta et al., 2014) and *P. brasilianum,* which is a new world monkey quartan malaria parasite diagnosed in humans in the Venezuelan Amazon (Lalremruata et al., 2015).

Malaria is seen worldwide and is among the world’s deadliest infections, with *P. falciparum* responsible for most of the mortalities associated with malaria (Aguiar et al., 2019). Moreover, malaria is one of the diseases that has left a genetic mark in human history with the prevalence of genetic variations, such as thalassemia, sickle-cell disease, glucose-6-phosphate dehydrogenase deficiency and many other human defects traceable to malaria (Bynum, 2008).

Malaria is still endemic in many countries and the current control measures worldwide seem to be insufficient (Espinoza, 2019). For the year 2020, WHO reported 241 million

cases of malaria globally, which is 14 million cases higher than 227 million cases reported in the previous year 2019. This increase was attributed to the disruption of malaria-related activities caused by the ongoing Covid-19 pandemic (WHO, 2021).

The 22% reduction in malaria cases seen over the past 10 years, has resulted in a 40% decrease in mortality in Africa (WHO, 2018e), but this progress has now stalled or even been reversed in some countries. Eleven countries accounted for 70% of the world malaria cases 2017 and ten of these countries were in sub-Saharan Africa and this is worrisome (WHO, 2018e).

Over the last two decades malaria control and elimination had received massive support by the international communities especially in sub-Saharan Africa, where the use of indoor residual spraying (IRS), artemisinin-based combination therapy (ACT), strengthening of healthcare systems and use of intermittent preventive therapy in pregnancy have resulted in a 52% decrease of disability adjusted life years globally between 1990-2016. However, despites this positive achievement, malaria still exerts a massive health and economic burden in sub-Saharan Africa, where the Global Burden of Disease 2016 report indicated that 10% of the disability adjusted life years is caused by malaria in sub-Saharan Africa (Amimo et al., 2019).

Although the use of indoor residual spray (IRS) and/or long-lasting insecticides treated nets (LLINs) used in malaria prevention has recorded great success in countries where such programs exist, these methods rarely led to the total elimination of malaria in the tropics. Their success is limited due to multiple factors such as insecticide resistance, inappropriate implementation, political instability as well as behavioural preferences in the vector population (Killeen, 2014).

1.2 Trends of Malaria in South Africa and Nigeria

South Africa has recorded positive progress in malaria control over the past 8 decades (Coetzee et al., 2013; SADOH, 2019), however malaria transmission is still seen in KwaZulu-Natal, Mpumalanga and low altitude areas of Limpopo, with sporadic transmissions periodically seen in the North-West province, mainly along the Molopo and Orange Rivers, with *P. falciparum* accounting for the majority of malaria cases in South Africa (SADOH, 2018). The transmission of malaria is seasonal with a peak period of transmission seen mainly between September to May (SADOH, 2018).

Currently the main vector responsible for this transmission is *Anopheles arabiensis*, a member of the *An. gambiae* complex. Other species in the complex include*, An. quadriannulatu sp and An. merus.* Historically as well as during the 1999/2000 malaria epidemic, *An. funestus* was the main vector implicated (Coetzee et al., 2013).

South Africa is in a malaria pre-elimination phase characterised by low malaria transmission (Moonasar et al., 2021).The malaria control programme has been operational since 1945 with many approaches used to eliminate malaria in South Africa (Coetzee et al., 2013), These approaches include: IRS for vector control, rapid diagnostic tests for rapid diagnosis and management, use of ACT, disease surveillance, epidemic preparedness and response and health promotion (Coetzee et al., 2013). However, the main interventional method is intensive indoor house spraying with dichlorodiphenyltrichloroethane (DDT) and pyrethroids (Brooke et al., 2013).

In Nigeria malaria is holoendemic and of public health concern, it imposes a significant morbidity and mortality in the country. It is the most widespread mosquito born disease and the number one killer disease in the country, even though it is ironically referred to as “common malaria” by the citizens, approximately 97% of the population are at risk, with 51 million and 207,000 annually reported cases and death respectively (Okwa, 2019; Afolabi et al., 2019).

The commonest and most virulent malaria parasite species in the country is *P. falciparum* and is responsible for the 95% of malaria cases; while *P. malariae* causes 5% of the infections. *Plasmodium ovale* infections in Nigeria are rare, with *P. vivax* completely absent not only in Nigeria, but also in west Africa. This is thought to be mainly due to the lack of the duffy antigen needed for the parasite invasion; although this is not always true due to the findings of sporadic cases of *P. vivax* isolates in a duffy antigen-negative patient (Oboh et al., 2018).

Historically malaria control is the oldest control program in Nigeria, having being operational since 1948, the main strategies of malaria control in Nigeria include: free distribution of long lasting insecticide treated nets (LLINs) which was initially approved to all children and pregnant women, but in 2009 it was scale up to include all ages, indoor residual sprays (IRS) approved since 2007 for prevention and control of epidemics, intermittent preventive therapy in pregnancy, home management of malaria which was adopted in 2005, and free artemisinin-combination therapies (ACTs) for all

under five years children and highly subsidized ACTs for other age groups in public hospitals. However, these strategies have not produced an optimal result, as the country failed to achieve the Abuja, and Roll Back Malaria targets (RBM) and presently Nigeria is trailing far behind in malaria control (Chukwuocha, 2012; Amzat, 2011; Maduka, 2018). Recently Nigeria has added WHO recommended seasonal malaria chemoprevention for children aged 3-59 months (Ward et al., 2022).

Also, anaemia is a common complication of malaria, although it has many causes. In South Africa severe anaemia is defined as a haemoglobin concentration less than 7g/dl or a haematocrit of less than 20% (SADOH, 2019). The prevalence of anaemia among all South African citizens that are older than 15 years of age was reported to be at 17.5%, where it is considered to be a moderate public health problem in women and mild public health problems in males (Shisana et al., 2014; SADOH, 2019).

The mechanism of anaemia in a malaria-infected patient is complex. However, the destruction of parasitized and uninfected RBCs (haemolysis), unregulated cytokines stimulations such as tumour necrotic factor, interleukin-10 and bone marrow dysfunction have been reported to be mechanisms of anaemia (Abdulkareem et al., 2017; SADOH, 2018). Additional known aetiologies of haemolytic anaemia are known to be associated with *Plasmodium* infections, namely, as a possible complication of concurrent glucose-6-phosphate dehydrogenase deficiency, severe parasitaemia, or use of parenteral antimalarials. In the case of 'severe parasitaemia', haemolysis occurs during the intra-erythrocytic stage of the parasites' life cycle; where at the end of the infection cycle, the red blood cells rupture resulting in a reduced number of functional red blood cells. As the parasitaemia increases, the severity of anaemia worsens as more infected red blood cells lyse (Menendez, Fleming, Alonso, 2000). In some cases of patients receiving parenteral artemisinin, they have been affected by episodes of anaemia after the clearance of the protozoal infection. These episodes are known as post- artemisinin delayed haemolysis (PADH). This is linked to the destruction of circulating parasitized red blood cells from which, after artesunate therapy, the parasites have been removed by "pitting" in the spleen, thereby deemed as once-infected red blood cells (Sardar et al., 2021). The haemolysis can occur anytime between a few days to four weeks after receiving the medication. Appropriate therapy is required to rectify patient haemoglobin levels to reduce the risk of death.

1.2.1 Malaria vectors in South Africa

In South Africa various *Anopheles* species have been identified including mosquitoes (Table 1.1) belonging to the *An. gambiae complex* and the *An. funestus* group (Christian *et al.*, 2018*)*. *Anopheles funestus* and *An. arabiensis* have been reported to be resistance to insecticide mainly in northern Kwazulu-Natal (Christian et al., 2018; Munhenga et al., 2022). The propoxur carbamate drug resistance in *An. funestus* is of epidemiological interest due to its higher intensity in malaria transmission as seen in 1996 to 2000 malaria epidemic in South Africa; the mechanism of propoxur carbamate drug resistance was believed to be a result of cross resistance to pyrethroid insecticide which occurred due to the higher level of mixed function oxidases which is the enzyme responsible for the detoxification of pyrethroid in mosquitoes (Brooke et al., 2001).However, the pyrethroid resistance *An. arabiensis* are not of much epidemiological significant because of its low intensity in malaria transmission (Samuel et al., 2018b; Gillies and Coetzee, 1987; Gillies and De Meillon, 1968). Currently, the primary vector responsible for the transmission of malaria in South Africa is *An. arabiensis,* while *An. merus, An. parensis* and *An. vaneedeni* are thought to act as secondary vectors (Christian et al., 2018). However, most researchers believed these species becomes accidently infected with malaria parasites since they mainly feed on animals (Maharaj et al., 2019; Burke et al., 2019a; Burke et al., 2017; Dandalo et al., 2017).

Table 1.1: *Anopheles* species collected by the vector surveillance team in South Africa in 2018 (Samuel et al., 2018b).

***Anopheles* species complex, group or other**	***Anopheles* species**	
An. gambiae complex	*An. arabiensis* *An. merus*	*An. quadriannulatus*
An. funestus group	*An. leesoni* *An. parensis* *An. rivulorum*	*An. rivulorum-like* *An. vaneedeni*
Other *Anopheles* species	*An. coustani* *An. demeilloni* *An. listeri* *An. marshallii* *An. pharoensis*	*An. pretoriensis* *An. rhodesiensis* *An. rufipes* *An. squamosus* *An. tenebrosus*

The main vector control intervention in South Africa is indoor residual spray (IRS) which was known to mainly protect people while indoors, however the current vectors like *An. arabiensisis*, *An. merus* display opportunistic feeding and resting behaviours (Gillies and De Meillon, 1968; Gillies and Coetzee, 1987). Their ability to also feed and rest indoors as well as outdoors reduces the efficacy of indoor vector control measures (Samuel et al., 2018b; Dandalo et al., 2017). In view of the necessity to break the transmission circle to achieve a complete malaria elimination in South Africa there is need to deploy a measure that protect people while outdoors, enhancing the use of mosquito repellents can be a good complementary measure to the currently used vector control measures in the country.

1.2.2 Malaria vectors in Nigeria

Similarly in Nigeria the main malaria vectors belongs to the *An. gambiae* complex (*An. gambiae s.s.* and *An. arabiensis*) and *An. funestus* group (FMOH, 2014). The *An. gambiae s.s*. and *An. arabiensis* typically breeds in temporary bodies of fresh water such as ground depressions and pools, while the *An. funestus* breeds in a permanent and semi-permanent water with an emergent vegetation such as large ponds and swamps (Gillies and De Meillon, 1968). These vectors are seen all over the country, stretching from the mangrove and coastal areas at the southern part to the Sahel region at the northern part of the country (FMOH, 2014; Adigun et al., 2015).

Anopheles melas, a member of *An. gambiae complex* breeds in salt water and is found in the mangrove and costal region of the south-south and southwestern part of Nigeria (Amadi et al., 2015; FMOH, 2014). *Anopheles gambiae s.s.* feeds on humans and rest indoors (endophilic), it has a sporozoites rate of 0.2% to 11.8% (FMOH, 2014). In contrast *Anopheles arabiensis* rest outdoors (exophilic) and feed on both animals and humans, it has a sporozoite rate of 0-4.8% (Amadi et al., 2015; FMOH, 2014). *Anopheles funestus* has an infection rate of 1.2% to 2.3%, it rests indoors and feeds on both humans (FMOH, 2014). When the different malaria vectors co-exist in a country, the infection rate was always higher *in An. gambiae s.s.*, followed by *An. funestus* and *An. arabiensis* (FMOH, 2014). Furthermore, infection during the wet season is mainly due to the *An. gambiae s.s.,* while during the dry season is mainly due to the *An. arabiensis* (FMOH, 2014).

Resistance of these vectors to some insecticide was also reported in Nigeria mainly at the northern and southwestern parts of the country (Atting et al., 2019; Awolola et al.,

2018). *Anopheles gambiae s.s.* was found to be resistant to DDT, pyrethroids and carbamates, *An.funestus* was resistant to DDT and dieldrin, while *An. arabiensis* was resistant only to pyrethroid (Atting et al., 2019; Djouaka et al., 2016; Awolola et al., 2018).

1.3 Life cycle of malaria parasite

The life cycle of *Plasmodium* parasites is very complex, but it can be simplified in to two phases which include: the asexual cycle that occurred in human and the sexual cycle that occurred in the mosquito. The two cycles are presented here in ten stages for easy comprehension (Figure 1.1) (Klein, 2020).

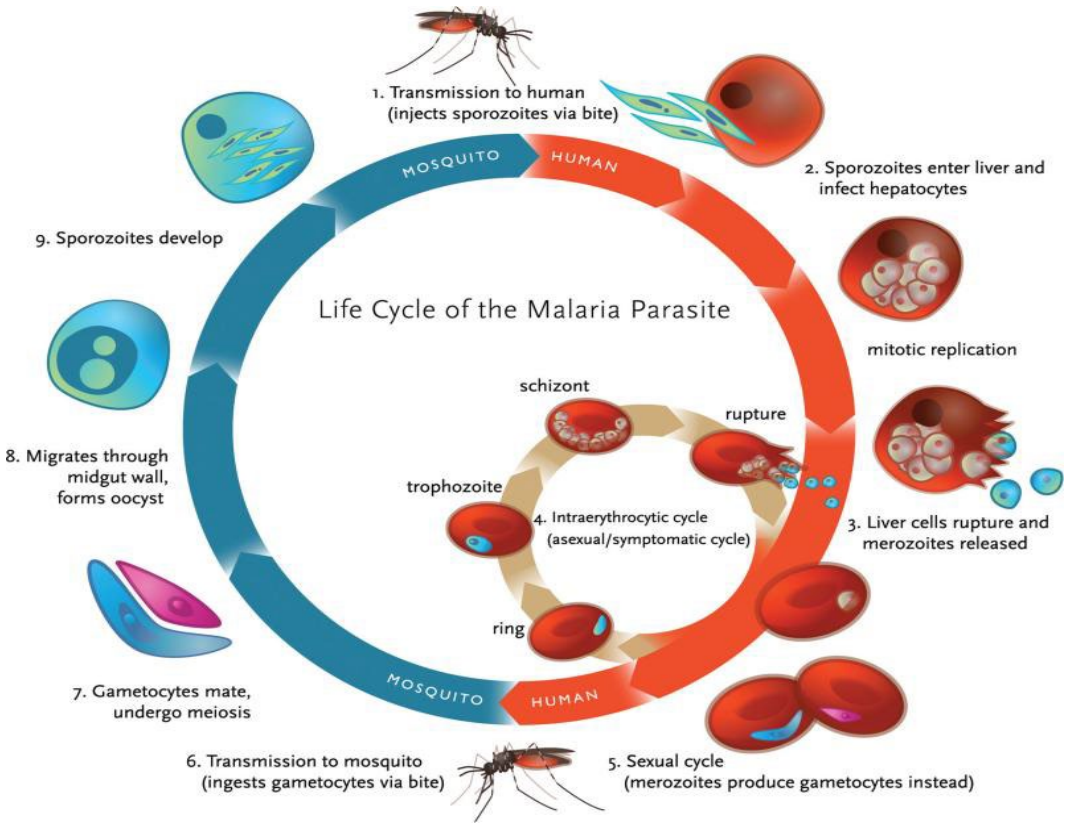


Figure 1.1: Life cycle of malaria parasite (Klein, 2012).

1. The cycle begins when an infected female *Anopheles* mosquito feeds on a person, during which the malaria parasites, in the form of a *sporozoites* are injected into the blood stream.
2. The sporozoites are quickly transported into the human liver via blood circulation.
3. In the liver the sporozoites multiply asexually via mitosis over a period of 7 to 10 days.

4. Then the parasites in the form of a merozoites in vesicles are released from the liver and transported through the blood stream into the lungs. These vesicles then settle within the lung capillaries, where they later become disintegrated, releasing a free merozoites that invade the red blood cells. From this point, the beginning of the blood / intra-erythrocytic developmental stage.
5. While in the blood stream, the released free merozoites invade erythrocytes and multiply asexually via mitotic division through an intra-erythrocytic cycle consisting of the ring, trophozoite and schizont stages, resulting in the release of daughter merozoites from the lysed erythrocyte. This cycle is repeated several times if not appropriately treated, causing clinical symptoms each time the erythrocytes lyse to release the merozoites.
6. A small percentage of the intra-erythrocytic parasites develop into the male and female gametocytes to ensure the transmission of the parasite strain into new hosts.
7. During a subsequent blood meal by the female *Anopheles* mosquito on an infected person, it ingests the gametocytes which undergo further maturation into male and female gametes.
8. These matured male and female gametes fused within the mosquito to form a diploid zygote that developes into an actively mobile ookinetes. The latter stage then migrates through the midgut wall of the mosquito to form oocysts at the peripheral surface of the midgut.
9. Within these oocysts numerous sporozoites are formed and subsequently released into the body cavity of the mosquito and then migrate to the salivary glands.
10. The cycle then repeats itself once this infected *Anopheles* female mosquito feeds on its next human blood meal.

1.4 Vector control

Vector control has been defined by WHO as “measures of any kind against malaria-transmitting mosquitoes, intended to limit their ability to transmit the disease” (WHO, 2018d). In controlling the malaria transmitting vectors the main strategies that proved to be effective are the use of LLINs or IRS (Corrêa et al., 2019). It is recommended that any country with endemic malaria, should target the reduction of its malaria burden and enhance elimination; instead of introducing new methods to potentially

complement the deficiencies of existing interventions which may not succeed (WHO, 2019b; Corrêa et al., 2019; Yang et al., 2018).

The LLINs has been considered as one of the most effective and successful methods of vector control and attributed to 68% reduction of malaria burden in Sub-Saharan Africa between 2000 to 2015 (Njumkeng et al., 2019; Bhatt et al., 2015). However, to date no country has reported the desirable minimum target coverage of 80% per household who own one ITN for two people (Koenker et al., 2018).

IRS is widely used for malaria vector control to reduce malaria transmission (Zinszer et al., 2019) and involves spraying an insecticide onto the walls of at least 80% of the households in the target area (Zinszer et al., 2019). Between 2015 and 2018, a total of 68 countries was reported to be using IRS with various formulations of insecticides, including pyrethroids, organochlorines, carbamates, and organophosphates (WHO, 2018e; Zinszer et al., 2019).

Even though LLINs and IRS have been proven to be very effective, unfortunately these methods only provide protections while indoors and leave people unprotected when outdoors (Nguyen et al., 2018). As such to close this gap, WHO recommends the use of mosquito repellents for personal protection whilst outdoors, especially when in malaria endemic areas (WHO, 2019b). However, at present there is a lack of supportive evidence for public health protections, as such mosquito repellents are not recommended for mass deployment for malaria prevention (Nguyen et al., 2018; WHO, 2019b).

1.5 Mosquito repellents for personal protections

The word repellent was derived from the Latin verb *repellere* which simply means “to reject” (Islam et al., 2017a). However, repellent has been defined by WHO as any chemical or substance that causes mosquitoes to avoid the host skin (contact repellent) or inhibit mosquitoes from entering an area or a room (spatial repellent) (WHO, 2018d).

Mosquitoes has a sense of smell (Figure 1.2A) to detecting their host (Figure 1.2B), as well as oviposition sites and to locate nectar (Sukumaran, 2016). They detect humans through the olfactory cues released by humans, some of these olfactory cues include carbon dioxide, 2-butane, ammonia, mixed phenols, lactic acids, 1-octen-3-ol and carboxylic acids (Watentena and Okoye, 2019; Sukumaran, 2016; Ray, 2015).

It has been proposed that an odorant can be used to interfere with the ability of mosquitoes to detect their host, and this can be achieved in three ways (Ray, 2015). Firstly, as "*repellents*" which deters mosquitoes from the human host (push only) (Figure 1.2D); secondly. as an "*attractant*" that entices mosquitoes into a trap that is located at a distance from the human host (pull only); and thirdly, as "*maskers*" that blocks the attraction of mosquitoes to humans (Maskers) (Figure1.2C) (Ray, 2015). However, field studies have shown that repellents (push) is more effective in providing personal protection against mosquitoes than the other two methods (Mmbando et al., 2019). A combination of repellents push plus traps, popularly called the push–pull method, has been shown to be even more effective in reducing the mosquito biting pressure than either method alone (Ray, 2015; Mmbando et al., 2019).

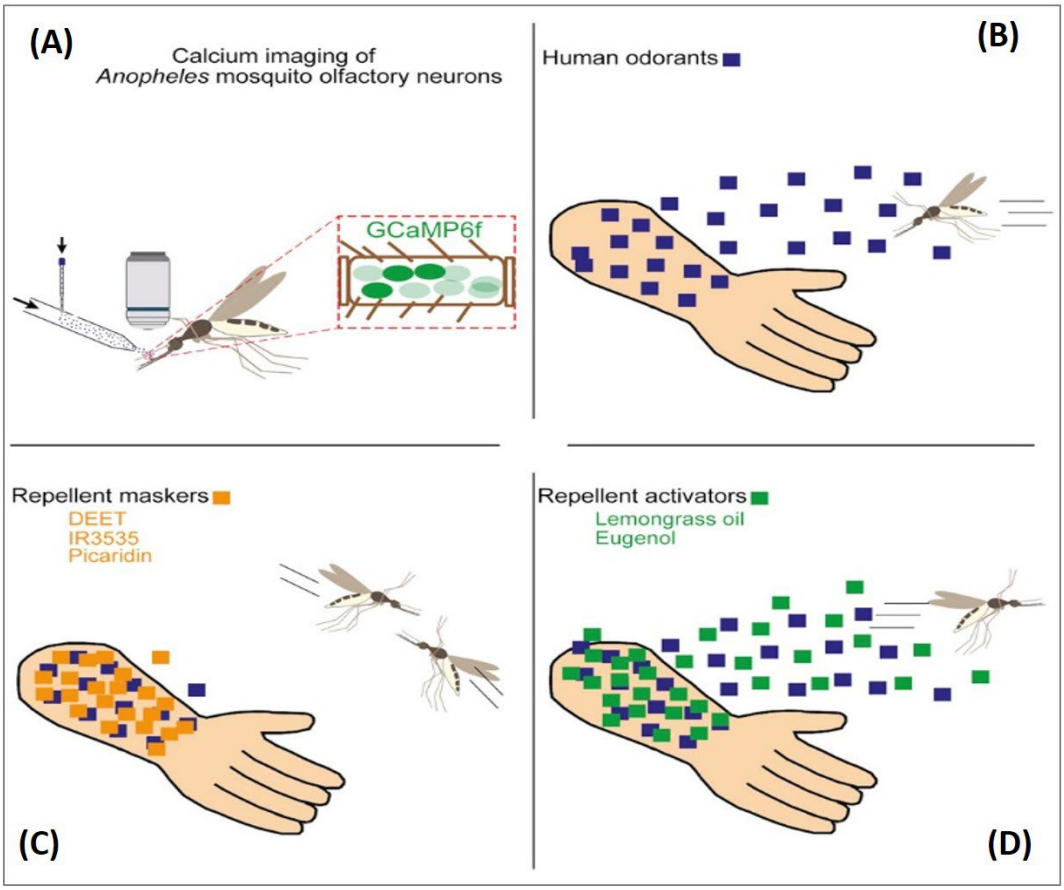


Figure 1.2: Mechanisms by which mosquito repellent act.
Calcium imaging of an *Anopheles* mosquitoes' olfactory neurons (A), how humans naturally attract mosquitoes (B), how synthetic chemicals worked as Maskers (C) and how natural products worked as repellents (D) (Afify et al., 2019).

Mosquito repellents is a reliable means of personal protection not just for the people residing in malaria transmission areas, but it is even more important for those visiting the malaria transmission countries (Khater et al., 2019). Generally, mosquito repellents can either be a synthetic chemical or a plant extract (natural products).

1.5.1 Synthetic mosquito repellents

Today there are many commercially available synthetic repellents on the market, however the main concern with the commonly used synthetic mosquito repellents like N, N-diethyl-3-methy-toluamide (DEET) is mainly related to their side effects, insensitivity, possible resistance, and carcinogenicity to mammals (Thireou et al., 2018). As a results of these concerns, many chemicals are still screened annually by researchers with the common aim of discovering a novel and ideal mosquito repellent (Thireou et al., 2018); where an ideal insect repellent should have various characteristics (Table 1.2) to be effective against mosquitoes and have a favourable safety profile. However, the ideal repellent product is yet to be discovered (Islam et al., 2017a; Tavares et al., 2018).

Table 1.2: Characteristics of an ideal repellent (Tavares et al., 2018)

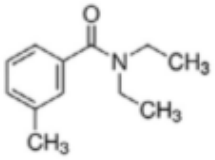
- protects an individual from biting insect as much as possible
- Reasonably longer duration of protection
- should work without any adverse effects
- should be chemically stable within the use conditions
- should have commercially affordable cost
- should be unscented or have a pleasant scent
- should have water and intense sweat resistance
- must not stain fabrics or clothing
- should be inert when in contact with plastics, acrylics, synthetics fibres and glass
- low skin penetration

1.5.1.1 N, N-diethyl-3-methy-toluamide

N, N-Diethyl-3-methy-toluamide (DEET) is regarded as the gold standard and the most common active ingredient in most of the commercially available insect repellents (Ho et al., 2019). It was first developed by the USA army in 1946 as a strategy to protect the personnel against the insect bite while on duty in an insect infested area (Ho et al.,

2019). DEET has been marketed for a personal protection against insect borne diseases since 1965 (Ho et al., 2019) and general information related to DEET is summarised in (Table 1.3). Several mechanisms of action of DEET have been proposed and are summarised in (Figure 1.3).

Table 1.3: Summarised up to date information on DEET insect repellent.

Characteristics	Descriptions
Chemical structure	 *N*,*N*-diethyl-3-methyl-toluamide, DEET, Diethyltoluamide, N,N-Diethyl-m-toluamide InChI=1S/C12H17NO/c1-4-13(5-2)12(14)11-8-6-7-10(3)9-11/h6-9H,4-5H2,1-3H3 SMILES=CCN(CC)C(=O)C1=CC=CC(=C1)C Molecular Formula= C12H17NO (NCBI, 2022)
General characteristics	DEET is an oily, volatile liquid, slightly yellowish at room temperature, insoluble in water, moderately soluble in petroleum ether, but very soluble in alcohol (Tavares et al., 2018).
Proposed Mechanisms of action:	▪ Feeding Inhibition (Ingestion) through activation of bitter taste gustatory neurons within the sensilla on the labella of the mosquito causing an inhibitory feeding response **(Figure 1.3A)** (Sanford et al., 2013; Sparks and Dickens, 2016). ▪ By stimulating insect smell (Olfaction) mainly via acetyl cholinesterase pathway (inhibition**) (Figure 1.3B)** (Wille et al., 2011; Swale et al., 2014; Legeay et al., 2018). ▪ As contact inhibitor because mosquitoes use their tarsi to sense DEET on contact to the DEET treated skin **(Figure 1.3C)** (Dennis and Vosshall, 2018; Dennis et al., 2019).
Formulations:	Lotion, Sprays**,** long release microencapsulated hydrogel, emulsion or hyphospheres (Edition, 2019), wrist or leg bands and treated clothing among others
Side effects and other concerns:	Burning sensation, blisters, skin eruptions, erythema, local necrosis, Seizures, Coma, death, irritants to the eyes and mucous membrane, Gulf war syndrome and plasticising effects (destroy plastics).
Safety precautions and Users advice	▪ Strictly follow the product level instruction, avoid for pregnant women and infants less than 6 months, can be used in children 2 to 12 years of age at a concentration not more than 10% (Tavares et al., 2018). ▪ The users should be careful about the claim duration of action by the manufactures as some DEET formulations may require frequent application every four hours for a complete protection (Edition, 2019).

	▪ It should not be applied and leftover at the bed time because of the fear of a serious skin reaction. ▪ Protect it from coming in to contact with plastic glasses or watch face.
Duration of an action	In normal use 50% DEET was generally thought to act for 3 to 4 hours, while using 100% DEET can extend the duration by one hour, that is 3 to 5 hours (Edition, 2019). Some products were claimed to act between 8 to 12 hours.
Efficacy and Toxicity profile	Most effective of all available repellents, unfortunately it is also the most toxic (Tavares et al., 2018).
Is it available in SA?	Yes
Products available on the South African market	

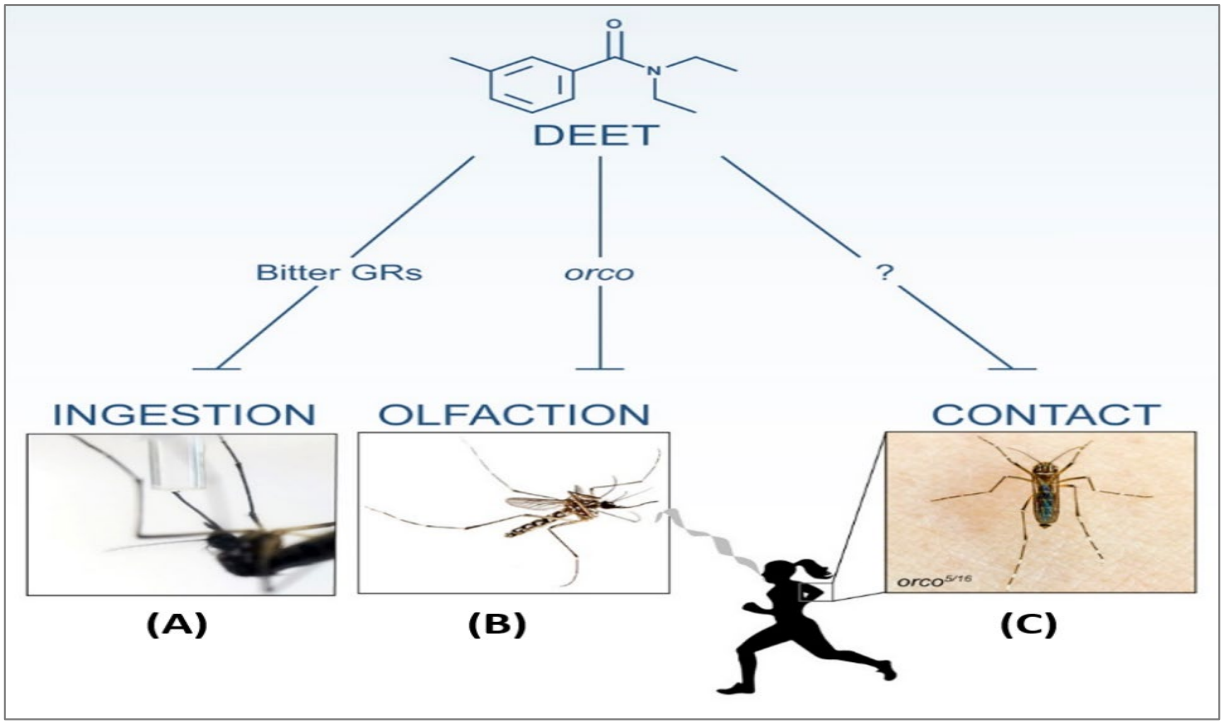


Figure 1.3: The three proposed mechanism of action of DEET action (Dennis et al., 2019).

Where: (A) Feeding Inhibition (Ingestion); (B) Olfaction inhibition via acetyl cholinesterase pathway; and (C) As contact inhibitor.

1.5.1.2 Insect repellent 3535

In an effort to produce an insect repellent that would be less toxic than DEET and comparable to both synthetic and natural repellents, over 30 years ago research led to the discovery of insect repellent 3535 (IR3535) by the German Merck group company (MERCK, 2019).It was initially named as Merck in 1999 (Hanem Fathy Khater et al., 2019).

IR3535 is a colourless, almost odourless, biodegradable compound (Figure 1.4F) that is commercially marketed in various pharmaceutical formulations including sprays, lotions aerosols and wipes, mainly at a concentration ranging from 7.5% to 19.5% (Tavares et al., 2018; Nguyen et al., 2018). The chemical structure of IR3535 is based on a natural substance called beta-alanine or chemically named, ethyl butylacetylaminopropionate according to the International Nomenclature of Cosmetics Ingredients (Tavares et al., 2018; Lo et al., 2018; MERCK, 2019). IR3535 has an estimated duration of action of two to eight hours, because of its exceptional skin tolerance and overall safety with a few repoted side effects including eye irritations, damage to clothing and plastics (Tavares et al., 2018; Iyigundogdu et al., 2019).

1.5.1.3 Picaridin

Picaridin (1-piperidinecarboxylic acid 2-(2-hydroxyethyl)-1-methylpropylester) is a piperidine analog developed by Bayer Pharmaceutical company in the 1980s (Figure 1.4D) (Hanem Fathy Khater et al., 2019). Physically, it is a colourless and nearly odorless liquid compound formulated commonly as a spray, lotion, cream, liquid, and solutions (Patel et al., 2016; Hanem Fathy Khater et al., 2019). This insect repellent was welcomed onto the market by the consumers because it does not feel greasy or sticky on application (Nguyen et al., 2018); and importantly it is effective against all three of the common mosquito vectors at a 20% concentration (Hanem Fathy Khater et al., 2019; Nguyen et al., 2018).

The exact mode of action of this repellent is still not well understood, but it has been postulated to act by providing a vapour barrier that prevents the insect from biting or affecting the olfactory sensory neurons of the insects (Nguyen et al., 2018). When deciding between DEET and picaridin as the repellent to use, most comparative studies only showed a small difference between the two compounds (Goodyer and Schofield, 2018). In comparison, other studies have shown superiority of picaridin over

DEET when applied at same dosage (Goodyer and Schofield, 2018). Moreover, most of the participants reported being more comfortable using picaridin rather than DEET (Goodyer and Schofield, 2018; Nguyen et al., 2018).

1.5.1.4 Other less commonly used synthetic repellent

One of the less commonly used synthetic repellents, namely (N, N-diethyl-2-phenyl-acetamide) (DEPA) (Figure 1.4E) that was developed around the same time with DEET, was shown to have similar efficacy, but was initially not accepted. However, it is now attracting the attention of researchers due to increasing concerns about the environmental safety and emergence of resistance to many currently available insecticide (Gupta, 2017; Balaji et al., 2017).

Another new and promising synthetic repellent in the field of entomology is ethyl anthranilate (Figure 1.4H) (Islam et al., 2017a). Which was shown to be nontoxic and presently is being considered as an effective and improved alternative to DEET (Islam et al., 2017b). It was also recently reported that butyl anthranilate, has more repellent activity than the ethyl anthranilate, and both can be an ecofriendly alternative to the existing toxic repellents (Zhao et al., 2019).

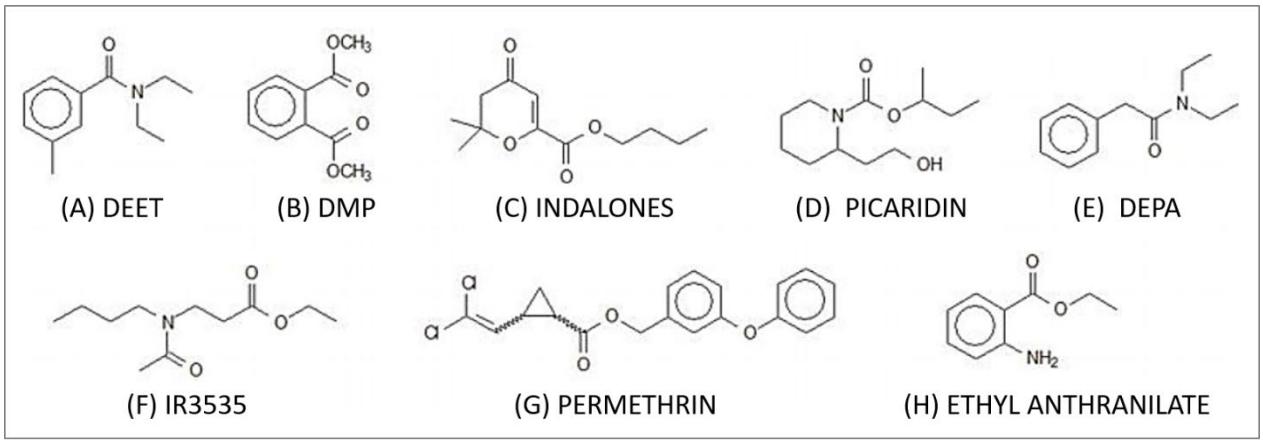


Figure 1.4: Chemical structures of some commonly used chemical repellents (Hanem Fathy Khater et al., 2019).
Where: (A) DEET: *N*,*N*-diethyl-3-methyl-toluamide; (B) DMP: Dimethyl phthalate; (F) IR3535: Insect repellent 3535; (E) DEPA: (N, N-diethyl-2-phenyl-acetamide).

1.5.2 Natural mosquito repellents (plants extracts and essential oils)

Nature remains an unlimited source of inspiration for healthcare therapeutic agents, as well as for scientific and technological innovations (Khater, 2017; Hanem Fathy Khater et al., 2019). An advancement in chemical science has led to the discovery and formulations of many synthetic mosquito repellents (Mukherjee and Ghosh, 2020). However, indiscriminate and continuous use of these synthetic products often results in adverse effects in the patient, as well as some deleterious effects on the non-target population. With the ultimate possibility of the development of resistance to these inappropriately administered/used repellents (Kim et al., 2020). These problems have pushed researchers to continue to search for simple, effective, eco-friendly, and sustainable repellents to control the malaria vector (Mukherjee and Ghosh, 2020; Kim et al., 2020).

To achieve this goal, researchers are currently exploring the possible use of natural substances, ranging from the plant extracts (Pawar et al., 2019), plant essential oils (Trongtokit, et al., 2005b); cow dung (Mukherjee and Ghosh, 2020), and also the possible use of elephant dung as a mosquito repellent (Petchimuthu et al., 2019). Historically, more than 60 plants belonging to 30 families have been used in Africa in various forms to repel mosquitoes, these plants are commonly used as smoke by burning the plant parts, by crushing then applied to the body or by hanging the plant inside the room or house to repel the mosquitoes (Pavela and Benelli, 2016). To highlight a few of the more commonly used natural mosquito repellent, including citronella, catnip oil and eucalyptus are summarised below.

1.5.2.1 Citronella

The word citronella was derived from the French word “citronelle”, which denotes any of the various plants whose herbs have a strong lemony smell (LEXICO, 2020). It was first used in the early 19th century by a British botanist, mycologist and pharmacologist called Samuel Frederick Gray (1766-1828) (FirstNature, 2011).

The citronella essential oils are extracted from the leaves and stems of different species of lemon grass (*Cymbopogon* Species) (Cerceau et al., 2020). The commonly available formulations of citronella-based mosquito repellents in the market include spray, wrist bands, oil and lotion and are usually found at a concentration between 14 to 50% (Patel et al., 2016). The citronella-based mosquito repellents are generally safe

to use, however because of its higher volatility the protection period is usually short, and it required frequent application (Agrawal et al., 2017). The researchers are now busy trying to develop a sustained released formulations of citronella oil-based repellent to prolong protection time and reduce the frequency of applications (Agrawal et al., 2017; Songkro et al., 2018; Bezerra et al., 2019).

1.5.2.2 Catnip oil

The catnip essential oil is extracted from the *Nepeta cataria* plant (Setzer, 2016). Apart from it being a well-known cat stimulant, it has many other functions which include amongst others, being an insect repellent, allelopathic, analgesic, anti-atherosclerotic, antifungal, antiviral, and spasmolytic (Tisgratog et al., 2016; Reichert et al., 2019; Baranauskienė et al., 2019). The main active ingredient of the catnip essential oil is nepetalactone, which occurs in two diastereomeric isomers (Z-E nepetalactone and E-Z nepetalactone) (Simon et al., 2019).

A 20% concentration of catnip essential oil has been shown to have a repellent activity of 100% against *An. stephensis* (Amer and Mehlhorn, 2006). In addition, a dose dependent efficacy against *An. gambiae*, at tested doses of 0.01mg, 0.1mg and 1mg have a repellency of 17%, 97% and 100%, respectively (Birkett et al., 2011)

1.5.2.3 Oil of Eucalyptus

Eucalyptus is a short, woody plant seen mainly in tropical regions (Asadollahi et al., 2019). It represents an important class of plant species as the essential oil has been widely commercialised because of its therapeutic properties (Asadollahi et al., 2019; Tian et al., 2020). The eucalyptus essential oil-based mosquito repellent is available in various formulations which include lotion, solution, spray, oil, wrist band, patch, and oil, where the topical application has been shown to provide better protection than the wrist band and patch (Patel et al., 2016). The eucalyptus essential oil-based repellents provide protection only for a short period of time and requires frequent application which is troublesome to consumers (Webb and Hess, 2016). However, it was discovered that the hydroxylated product of eucalyptus essential oil, namely, p-methane-3,8-diol (PMD) provides longer protection for up to 5 hours (Webb and Hess, 2016; Nguyen et al., 2018).

1.5.2.4 Other plants extract with insect repellent activities

There is an increasing demand for a safe, cost-effective, pleasant smelling, and eco-friendly mosquito repellent by consumer (Asadollahi et al., 2019; Ma et al., 2019). This could be provided by fully evaluating plant extracts and essential oils (Eden et al., 2020). Some of these tested plants with repellents activities include amongst others: olive oil (*Olea europoe*), frankincense (*Boswellia spp*), peppermint (cross breed of *Mentha spicata* and *Mentha aquatica*), thyme (*Thymus serpyllum*), ylang ylang (*Cananda odorata*), tergetes (*Tergetes minuta*), turmeric, java citronella (*Cymbopogon winterianus*), orange oil (Asadollahi et al., 2019; Eden et al., 2020; Pavela et al., 2020). The exact mode of action of the plant based essential oil is still under research, however it has been proposed that, the essential oil interfered with the mosquito's olfactory receptors (Asadollahi et al., 2019).

1.6 Malaria Chemoprophylaxis

The control of mosquito vectors (Section 1.4) and avoiding mosquito bites to prevent malaria infections (Section 1.5) are two of the main mechanisms of malaria chemoprophylaxis (SADOH, 2018; WHO, 2019b). The widespread distribution of drug-resistant malaria parasites, coupled with the side effects associated with some of the antimalarial medications, necessitates the need for controlling mosquitoes. The use of antimalarial prophylaxis and most importantly the use of non-drug measures are critical to in the prevention of a malaria infection (SADOH, 2018). There are five key components that make up a good and comprehensive malaria prevention strategy acronym as "ABC of malaria prevention". Where "A": stand for awareness and assessment of malaria risk, "B": avoidance of mosquito bites, "C": compliance with chemoprophylaxis when indicated, "D": early detection of malaria disease and "E": effective treatment (Van Zyl, 2016; SADOH, 2018).

Tourists should ensure they are well informed about the malaria status and medications needed when travelling to a malaria endemic area and whether they should travel there or not (Goodyer, 2019; RBM, 2019). Furthermore, it is also important for healthcare professionals (HCPs) to be well informed on how to manage high risk individuals, like immunocompromised people (HIV/AIDS, immunosupressed), young children, the elderly, and pregnant women (SADOH, 2018).

To prevent mosquito bites, personal protection with mosquito repellents is highly recommended, especially with DEET containing products (Goodyer, 2019). Those that cannot use DEET (Table 1.3), PMD or icaradin are good alternatives, however natural repellents should be used with caution because of their low efficacy and unreliability in avoiding mosquito bites (Goodyer, 2019). People should be aware about the feeding behaviours of the *Anopheles* mosquito, which is from dusk to down, and people should preferably wear long sleeves, trousers, socks and if possible, should sleep under a LLINs (SADOH, 2018).

Chemoprophylaxis should be recommended only for those that needed them (FMOH, 2014). The decision to prescribe chemoprophylaxis is complex and mainly depend on the area to be visited, the higher risk group individuals and whether the traveller is at higher risk of being exposed to the mosquito bites and developing malaria (SADOH, 2018).

Currently in South Africa and Nigeria three medications are recommended for chemoprophylaxis which include: doxycycline, atovaquone-proguanil and mefloquine (CDC, 2021). Strict adherence with the dosing regimen is highly recommended for a good protection (Table 1.4) (SADOH, 2018). Blind recommendations of the chemoprophylaxis are highly discouraged because of the deleterious side effects of these medications if prescribed inappropriately, as such the HCPs are advised to use a guideline to make such a decision (SADOH, 2018).

Table 1.4: The recommended regimen for the approved malaria chemoprophylaxis in South Africa (SADOH, 2018).

Mefloguine (Weekly)	Start at least one week before entering a malaria area, take once weekly while there and for four weeks after leaving the malaria area.
Doxycycline (Daily)	Start one day before entering a malaria area, take daily while there and for four weeks after leaving the malaria area.
Atovaquone-proguanil (Daily)	Start one to two days before entering malaria area, take daily while there and for seven days after leaving the area

1.7 Diagnosis and Management of malaria infections

Prompt diagnosis and appropriate management of a malaria infection can save lives. As such the guidelines from WHO and those prepared for South Africa are an essential read for all HCPs, especially Medics, Nurses, and Pharmacists. Continuous education and updates on the current and potential diagnostic methods (Section 1.6.1) and those agents required to prevent and manage (Section 1.5 and 1.7) infected patients should be well known to all HCPs. According to the South African Department of Health, a positive laboratory test should be obtained before treatment is prescribed (van Zyl, 2016).

1.7.1 Malaria diagnosis

While reviewing the hope for a world-free malaria by the year 2030, WHO has emphasized the importance of early and accurate diagnosis of malaria as a main strategy for malaria management and surveillance (WHO, 2015a). The goal of a malaria-free world is in-line with one of the global sustainable development goals (SDGs) designed to address morbidity and mortality of several pathologies. Within SDGs 3, it is aimed to “Ensure Healthy Lives and Promote Well-being for all and all ages” and thereby do what is necessary to eradicate malaria globally by the year 2030 (SDGs, 2017; Onile-ere et al., 2016).

As such WHO recommends prompt testing of all malaria suspected cases by using either a rapid diagnostic test (RDT) or microscopy (WHO, 2018b). It is recommended that patients exhibiting malaria symptoms, preferentially start treatment following a positive diagnostic result to exclude possible misdiagnosis through history and clinical examination of a patients and due to the non-specific presentations of the disease (SADOH, 2019b). However in the event of the unavailability of a RDT diagnostic kit or equipment required for microscopy, the HCPs should use their clinical judgement, by considering the severity of the patients’ clinical conditions and possible history of an exposure to the malaria parasite (SADOH, 2019).

1.7.1.1.1 Clinical diagnosis

Clinical diagnosis is referred to as presumptive diagnosis and is considered the most rapid and cheapest way to diagnose malaria in remote areas in Sub-Saharan Africa, where laboratory support is not always available (Onile-ere et al., 2016). However, this method is not always accurate, as it is based on the combinations of the patients’

symptoms and signs related to malaria; which are not always specific to malaria as they are associated with many other human diseases (Mfuh et al., 2019; Wilson, 2013; Wogu and Nduka, 2018). Nevertheless, it is the most useful diagnostic method recommended in under 5-year-old children, as in this age group, malaria can easily progress to a severe form and potentially be fatal if treatment is delayed. WHO does however recommend that the use of clinical diagnosis coupled with RDTs should be used in all cases before the commencement of an antimalarial therapy (WHO, 2016; Onile-ere et al., 2016). It is essential all precautions are taken, and guidelines are followed to prevent the development and spread of resistance to available antimalarial medications (WHO, 2018b; Moyeh et al., 2019).

1.7.1.1.2 Microscopic methods

Microscopic examinations of a thick and thin blood films stained with either Giemsa, Field's or Wright's stains using Romanowsky staining techniques, has been described as the gold standard method in diagnosing malaria (Mbakilwa et al., 2012). The combination of a well-prepared blood smear, a well-trained laboratory personnel, coupled with a good microscope is essential to establish the presence or absence of the malaria parasite and the species involved (Tangpukdee et al., 2009). In addition, the microscopic examination of a thin blood smear can also help in quantifying the level of parasitaemia (Amir et al., 2018; Tangpukdee et al., 2009).

Furthermore, apart from the conventional light microscope, the era of technology has enabled the inventions of more developed and sophisticated methods to detect the presence of a low level parasitaemia and prevent false-positive results. These include the quantitative buffy coat method (QBC) (Vaisakhi et al., 2017; Chigurupati and Srinivas, 2016) and Partec malaria RDTs which are very sensitive and require less training to be used (Birhanie, 2016).

In addition, there are advantages of using an automated microscope that uses artificial intelligence to detect malaria on a slide, thereby excluding the problem of untrained personnel and eliminating any potential subjective analysis influenced by the level of parasitaemia and equipment quality (Torres et al., 2018a; Jan et al., 2018; Amir et al., 2018); This method maybe costly to setup, but is cost effective, widely used and cheaper than the molecular techniques (Amir et al., 2018).

1.7.1.1.3 Rapid diagnostic tests

Fingerprick RDTs are now seen as a complement to the gold standard traditional malaria diagnosis by microscopy (Amir et al., 2018). The various RDT products work via the same principle except for the variations in targets and formats, with some able to detect one species (*P. falciparum or P. vivax*) or multiple species (*P. falciparum, P. vivax, P. malariae* and *P. ovale).* Malaria RDTs detect specific malaria-antigens released into the blood of infected individuals by binding them to dye-labelled antibodies to produce a visible band on the nitrocellulose strip (WHO, 2018a). The three targeted malaria parasites antigens that are used in RDT include: histidine-rich protein two (HRP2) which is specific for detection of *Plasmodium falciparum (Murray et al., 2008). Plasmodium* lactate dehydrogenase and aldolase these two antigens are used to detect all the human malaria causing parasites species, hence also called pan-*Plasmodium* antigens (Murray et al., 2008; Willie et al., 2018).

The recent development in malaria rapid diagnosis is the ultra-RDT, which has an improved sensitivity and can detect an infection at parasites load ten times lower the conventional RDT (Das et al., 2017). In addition, it can also detect an infection 1.5 days earlier than the conventional RDT (Mwesigwa et al., 2019).

1.7.1.1.4 Molecular diagnostic methods

Molecular diagnostic technologies such as polymerase chain reaction (PCR) are becoming the new gold standard method in malaria diagnosis (Amir et al., 2018). It is more sensitive than microscopy and RDT with real-time quantitative PCR (qRT-PCR) able to detect a low % parasitaemia in the blood sample and allows for the identification of the parasite species present in the clinical sample (Haanshuus et al., 2019; Mfuh et al., 2019; Ngasala et al., 2019; Tambo et al., 2018). Results obtained from the PCR are not subjective which also make it superior to the conventional microscopy (Amir et al., 2018). However, the drawback of PCR is that it is expensive, required laboratory cleanliness and cumbersome, which make*s* it difficult to be used in a remote area (Amir et al., 2018).

Other molecular technologies include: quantitative nucleic acid sequence-based amplification (QT-NASBA) that allows for the detection of gametocytes at parasites densities significantly below the threshold of conventional light microscope (Pett et al., 2016). In addition, loop mediated isothermal amplification (LAMP) is highly sensitive

technique that does not require much training to be operated (Charpentier et al., 2019; Kudyba et al., 2019), with qRT-PCR and immunofluorescence assays both highly efficient methods for gametocyte detection (Gruenberg et al., 2019).

1.7.1.1.5 Non-invasive methods

Non-invasive diagnostic tools are an exciting and innovative advance in diagnosing malaria (Berna et al., 2015). Several studies have been undertaken to investigate the potential of using volatile organic biomarkers released from pathogen-infected patients in the diagnosis of malaria (Chai and Chua, 2021). .Emami *et al.* (2017) found that mosquitoes are attracted more to malaria-infected patients due to the release of a parasite-derived isoprenoid called (E)-4-hydroxy-3-methyl-but-2-enyl pyrophosphate (HMBPP); where the latter was found to indirectly increase the production of carbon dioxide, several monoterpenes, and aldehydes from human red blood cells. In contrast, Berna et al. (2015) reported on the release of carbon dioxide, isoprene, acetone, benzene, cyclohexanone, and 4 thioethers (allyl methyl sulfide, 1-methylthio-propane, (Z)-1-methylthio-1-propene, and (E)-1-methylthio-1-propene) in the breath of malaria-infected patients. Based on this observation, Berna et al. (2015) investigated a promising simple, non-invasive tool to detect thioether in the breath of suspected malaria-infected patients', that was not associated with any other human disease. Berna et al. (2015) found a direct correlation between specific malaria-associated volatiles, such as thioether and the parasitaemia of the blood.

Based on the differential odour of uninfected and infected patients, the extremely sensitive olfactory system of dogs has used to detect malaria-emitted volatile compounds from foot odour of children infected with malaria (Guest et al. 2019; Kasstan et al., 2019). The use of bio-detection dogs for medical diagnosis purposes as an alternative to molecular tools has been proven to be feasible as a mobile diagnostic approach for detecting individuals with asymptomatic malaria.

Furthermore, various samples such as urine and ethanol-preserved faeces have been used to detect the *Plasmodium* parasites (Oyibo et al., 2017; Al-Shehri et al., 2019). A urine malaria test is another non-invasive technology that has been found to detect the *Plasmodium falciparum* specific histidine-rich protein-2 (HR-2); where the latter is a poly-histidine protein or fragments found in the urine of a febrile patients (Oyibo et al., 2017). The field trial conducted by Oyibo et al. (2017) to evaluate the efficacy of the urine malaria test showed that it is highly promising, with a sensitivity and specificity

comparable to that of microscopy and RDT. Whilst in a schistosomiasis-malaria co-surveillance study, Al-Shehri et al. (2019) reported that using ethanol-preserved faeces sampling with rtPCR analysis provided a satisfactory diagnostic performance in estimating the mean prevalence upon direct comparison with field-based point-of-care-RDTs. Although analysis of ethanol-preserved faeces was judged inferior to that of dried blood spots.

When fully evaluated and validated, the non-invasive malaria diagnostic methods will serve as an alternative in a situation in which the blood sample are difficult to obtain, as often encountered by the HCPs in paediatric patients (Amir et al., 2018).

1.7.2 Treatment of malaria

When dealing with a confirmed positive malaria case, it is always of critical importance to firstly differentiate if the index case is uncomplicated or severe malaria (FMOH, 2005), as this will establish the severity of the illness to guide the overall management plan (SADOH, 2018). Infections with *Plasmodium* parasites result in many effects ranging from asymptomatic parasitaemia, uncomplicated malaria, severe malaria to death (Plewes et al., 2019). The ultimate goals for the management of malaria are mainly to reduce morbidity and mortality, to prevent disease progression into severe malaria, to eliminate subclinical cases as such prevent further transmission (SADOH, 2018). Also, part of the goal of malaria treatment is to prevent or limit the development and spreads of resistance to antimalarial medications (SADOH, 2018; WHO, 2018c).

In management of malaria, a higher index of suspicion is required, as a key driver to the early diagnosis (SADOH, 2019). In a classical case, malaria commonly presents with fever, body pains, rigors, and headache, however these symptoms are non-specific and not limited to malaria only. As such malaria may be confused with other diseases, more especially viral infections such as influenza and Covid-19 (SADOH, 2018; Gulen and Satar, 2020). Nevertheless, malaria should be suspected in any patients presenting to the health facilities with a history of a recent visit to malaria transmission areas or a residence of that area and having some of the following symptoms (Table 1.5) (WHO, 2015b; SADOH, 2018, 2019).

1.7.2.1 Treatment of an uncomplicated malaria

A patient can be considered to have uncomplicated malaria with a microscopic parasitaemia count of less than 4% or <3+, along with no evidence of organ dysfunction

detected through clinical examination or laboratory test (SADOH, 2018; 2019). The main purpose of treatment is to ensure rapid clearance of parasitaemia and to prevent progression of an uncomplicated cases into severe form of malaria or death (WHO, 2019d). According to both WHO (2019d), SADOH (2019b) and FMOH (2005), all patients diagnosed with uncomplicated malaria whether a child or an adult should be commenced immediately on ACT except for a pregnant woman in their first trimesters of pregnancy.

Table 1.5: Common symptoms and signs of malaria; source: South African National Guidelines for the Treatment of Malaria (SADOH, 2019b).

- Fever
- Chills
- Rigors
- Joint pain
- Lethargy
- Loss appetite in older children and adults
- Poor feeding in young children
- Abdominal discomfort
- Diarrhoea
- Nausea and vomiting
- Cough in young children
- Splenomegaly for patients in areas with higher intensity of malaria transmission

In South Africa and Nigeria, artemether-lumefantrine (Coartem™) is recommended for all cases of uncomplicated malaria for a period of three days (Table 1.6). Current evidence shows that it can also be used in the first trimester of pregnancy if the main regimen consisting of clindamycin plus quinine is unavailable (FMOH, 2005; CDC, 2018; SADOH, 2019b). Vomiting is considered to be one of the leading causes of treatment failure in uncomplicated malaria, as such for all patients with an uncomplicated malaria the first dose of the prescribed ACT should be taking in the hospital and observed for possible vomiting over a period of at least one hour (SADOH,

2019). Patient should be also advised to return to the hospital as soon as their condition does not improve (SADOH, 2019b).

Table 1.6: Dosage of artemether + lumefantrine recommended according to the patient weight in kilogram (SADOH, 2019b; FMOH, 2005).

Weight	Dosage	Total number of tablets
5- <15kg	1 tablet start, followed by 1 tablet after one hour, then 1 tablet b.d for the following 2 days	6
15- <25kg	2 tablets start, followed by 2 tablets after one hour, then 2 tablets b.d for the following 2 days	12
25- <35kg	3 tablets start, followed by 3 tablets after one hour, then 3 tablets b.d for the following 2 days	18
35-<65kg	4 tablets start, followed by 4 tablets after one hour, then 4 tablets b.d for the following 4 days	24
>65kg	Same with those above 35kg, though inadequate experience with this age group, indicate the need for a close monitoring.	24

Patients whose laboratory results show an infection with either *P. vivax*, *P. ovalae* or a mixed infection of any of these species with *P. falciparum* should be treated with primaquine for fourteen days to prevent relapse due to the hepatic stages of the parasite (SADOH, 2019b). However, primaquine should not be given to those with glucose-6-phosphate dehydrogenase deficiency, pregnant women, infants less than six months, and mothers breast feeding an infant less than six months of age (SADOH, 2018; WHO, 2019d).

1.7.2.1 Treatment of severe malaria

Severe malaria is a complicated form of malaria mainly associated with *P. falciparum* and is a medical emergency associated with a 10-40% mortality rate (Jauréguiberry, 2019).

However, with a prompt and effective treatment, especially when done at the highest level of care available, death can be averted (Jauréguiberry, 2019; SADOH, 2019b). WHO has developed a wide range of both clinical and laboratory features associated with severe malaria, where severe *P. falciparum* is defined as any patient with one or more of the severe features of malaria obtained from the history and clinical

examination or from laboratory tests (Table 1.7) (SADOH, 2019b). This is coupled with the presence of an asexual form of *Plasmodium* parasites in the blood and absence of any other identifiable alternative explanations of the patients' clinical condition (WHO, 2015b; SADOH, 2019b).

Table 1.7: Criteria for diagnosis of severe *P. falciparum* malaria (SADOH, 2019b).

Clinical	Laboratory
Impaired consciousness	Hypoglycaemia <2.2mg/dl or <40mg/dl
Multiple convulsion: > 2 episodes in 24 hours	Hyper parasitaemia
Jaundice	Haemoglobinuria
Prostration	Severe normocytic anaemia (Hb <7g/dl
Acute pulmonary oedema	or haematocrit <20%)
Acidotic breath or respiratory distress	Pulmonary oedema (Radiological)
Shock	Metabolic acidosis
Anuria	Hyperlactataemia
Abnormal bleeding	Serum creatinine >265mmol/l

All patients with severe malaria should be treated with parenteral artesunate (intravenous or intramuscular) for at least 24 hours given at 0, 12 and 24 hours, the treatment can be extended as a daily dose, until the patients can tolerate oral medications, then switch to ACT for a complete three-day course (WHO, 2015b). When artesunate is not available, artemether or quinine can be used, but artemether is prepared to quinine (WHO, 2015b; Esu et al., 2019; Mathiba et al., 2019). Children weighing less than 20kg should receive 3mg/kg body weight of artesunate, while those greater than 20kg should be given 2.4mg/kg body weight (WHO, 2015b; SADOH, 2019b).

1.8 Pharmacology of the common antimalarial chemotherapeutic agents

The antimalarial medications that are currently used for the treatment or prevention of malaria, belong to the four classes of antimalarial drugs viz: artemisinin derivatives, quinoline related compounds, antifolates and antimicrobials (Herchline and Simon, 2019; SADOH, 2018; 2019). It is pertinent to note that to date no single antimalarial compound has been discovered, that can eradicate all stages of the *Plasmodium*

parasite (Herchline and Simon, 2019). Many of the antimalarial chemotherapeutics agents used to prevent or treat a malaria infection act mainly at the erythrocytic phase of the malaria parasites lifecycle; however, a few agents act on the hepatic (pre-erythrocytic) phase (Rosenthal et al., 2021). The pharmacology of these commonly used classes of antimalarial drugs are discussed below.

1.8.1 Quinoline-related compounds

Historically the first antimalarial agent was reported in 17th century, which was extracted from the bark powder of the *Cinchona* tree found in South America (Martinez et al., 2018). Two centuries later, the quinine alkaloid was isolated and identified as the therapeutically active ingredient in the crude tree bark (Martinez et al., 2018). Around 1940's the first quinoline derivative was synthesised named plasmoquine, but because of its toxicity this drug was immediately replaced by primaquine (Figure 1.5) (Martinez et al., 2018). The chloroquine was then developed within the same decade with primaquine, and it becomes widely used, however the report of resistance to chloroquine during the Vietnam war led to the discovery of mefloquine (Martinez et al., 2018). Still the report of toxicity and resistance narrowed the used of mefloquine, as of today the most recently approved quinoline drug for the treatment of malaria is amodiaquine, while another drug named ferroquine is currently under Phase IIb clinical trial (Martinez et al., 2018; Stringer et al., 2019).

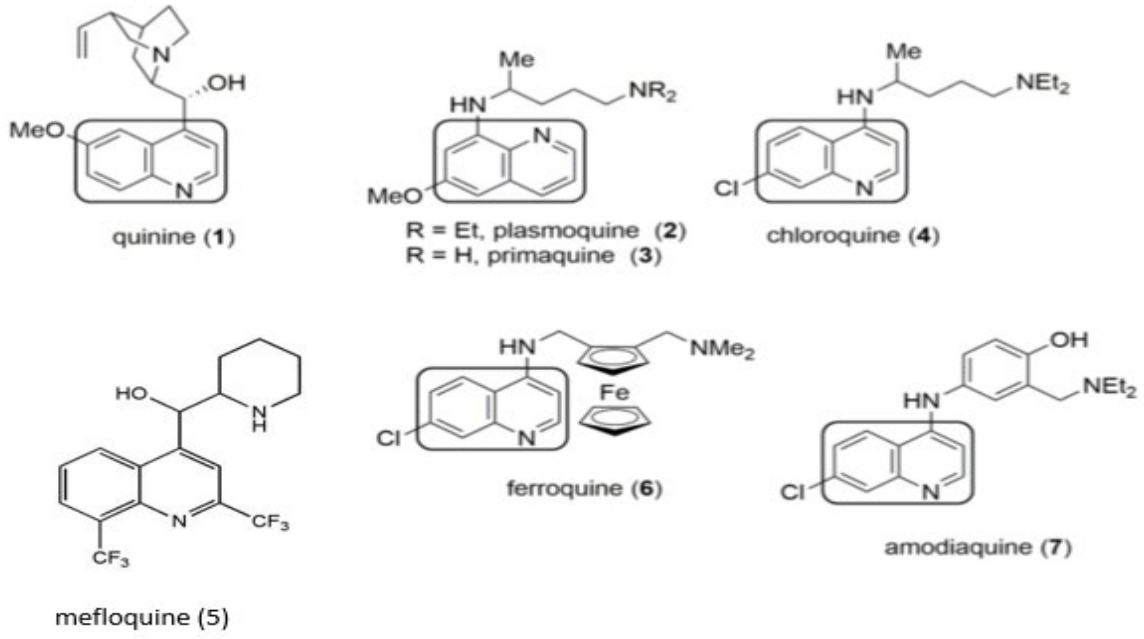


Figure 1.5: Quinoline derivatives with antimalarial activities (Martinez et al., 2018).

Some of the pharmacological activities of the quinoline derivatives include amongst others (Chu et al., 2019); antimalarial, anticancer (Li et al., 2019), antibacterial (Fu et al., 2019), antileishmanial and antitrypanosomal agents (Chanquia et al., 2019), and anti-inflammatory activities (Tseng et al., 2018).

In the field of malaria, the most used quinoline derivatives antimalarial drugs are chloroquine, quinine and mefloquine (Balamurugesan et al., 2019). The mode of action of quinoline antimalarials has been proposed to be the interference of haemoglobin digestion through inhibition of the crystallisation of haem to haemozoin. This process is critical for the survival of the malaria parasite, but the formation of the toxic haem-quinoline complex results in parasite death through oxidative damage and the formation of free radical that lyse the parasitic and red blood cell membranes (Balamurugesan et al., 2019).

Below is a brief pharmacology on the two commonly used and prototype drugs in the quinoline class of antimalarial drugs viz: Chloroquine and Quinine (cinchona alkaloid).

1.8.1.1 Chloroquine

Chloroquine, a 4-aminoquinoline is a very effective antimalarial drug that has been used for both the chemoprophylaxis and treatment of malaria (Goel and Gerriets, 2019). However, the report of a widespread *Plasmodium* parasite resistance has compromised it use in malaria treatment and prophylaxis (SADOH, 2019b). In South Africa, it is only used in the management of an infection of *P. vivax, P.ovale*, and *P. malariae* (SADOH, 2019); but it is still approved as the drug of choice in countries with chloroquine-sensitive malaria parasites (Rosenthal, 2021).

The oral formulation of chloroquine is almost completely and rapidly absorbed from the gastrointestinal tract and reaches it maximum plasma concentration within 3 hours before being renally excreted with an initial half-life of 3-5 days, and a terminal half-life of 1–2 months (Rosenthal, 2021). The most commonly reported side effects associated with chloroquine affect the gastrointestinal-, central nervous-, cardiovascular-systems and blood related side effects; where prolong used of chloroquine can lead to peripheral neuropathy, ototoxicity, retinopathy, and myopathy (Balamurugesan et al., 2019; Rosenthal, 2021).

Although chloroquine is safe even during pregnancy, still it is recommended for a safety precaution not be administered in a rapid large parenteral dose, because it may lead to cardiac or respiratory arrest (Balamurugesan et al., 2019). It is contra-indicated in patients with porphyria and psoriasis and should preferably not be used in those with retinal myopathy, visual field abnormalities and in a patient with renal and liver disease (Balamurugesan et al., 2019; Rosenthal, 2021).

1.8.1.2 Quinine

Quinine is a rapidly acting and highly effective blood schizonticides against the human malaria parasites and gametocidal against *P. vivax* and *Plasmodium ovale*, but not against *P. falciparum* (Rosenthal, 2021). Orally administered quinine is rapidly absorbed, reaching its peak plasma concentration within 1-3 hours (Rosenthal, 2021). A loading dose of 20mg/kg is often administered to patients with severe malaria to achieve a peak plasma concentration within a few hours, and then has a half-life of 18 and 11hours in malaria infected and healthy patients, respectively. Before being metabolised in the liver and excreted in the urine (Rosenthal, 2021).

The quinine and its dextrorotatory stereoisomer (quinidine) are usually associated with an adverse effect termed cinchonism, which is a constellation of symptoms that include: tinnitus, headache, dizziness, visual disturbances, nausea, and flushing (Pagar and Khandbahale, 2020; Rosenthal, 2021). These symptoms are usually mild and may not require drug discontinuation but can cause deafness and blindness if the plasma concentration exceeded therapeutic ranges (Pagar and Khandbahale, 2020).

Even though there is resistance to quinine with a report of decreased quinine effectiveness, especially in Southeast Asia and South America, intravenous quinine is still considered an effective alternative therapy in management of severe malaria when artesunate is not available in South Africa (Conrad and Rosenthal, 2019).

1.8.2 Antifolates antimalarial drugs

The antifolate antimalarial drugs inhibit the *Plasmodium* dihydrofolate reductase (DHFR) enzyme that is essential in the synthesis of purines and pyrimidine synthesis for parasite proliferation (Nattee et al., 2017). The DHFR enzyme inhibitors that are commonly used against malaria include pyrimethamine, trimethoprim and cycloguanil (the triazine active prodrug of proguanil) (Nattee et al., 2017).

These drugs are often used in combination with other drugs in the prophylactic treatment of malaria, such as proguanil with atovaquone (Nattee et al., 2017; SADOH, 2018; Rosenthal, 2021). The oral antifolate inhibitors are well, but slowly absorbed when administered orally, with the proguanil reaching a peak plasma concentration in 5 hours, with an elimination half-life of 16 hours which accounts for the daily dose regimen (Rosenthal, 2021).

1.8.3 Antimicrobials used in malaria management

Employing therapeutically available antimicrobial agents that have proven to be active against *Plasmodium* parasites act in an entirely different mechanism of action from that of the standard antimalarials and in doing so, alleviate the fear of cross resistance (Gaillard et al., 2016). The commonly used and approved antimicrobial agents in the field of malaria therapy in South Africa and Nigeria are doxycycline and clindamycin (SADOH, 2018; 2019; FMOH, 2014).

1.8.4 Artemisinin and artemisinin derivatives

Artemisinin are sesquiterpene lactones endoperoxide compounds isolated from *Artemisia annua* (Heller and Roepe, 2019). Artemisinin and analogues contain an endoperoxide bridge, which provides a very effective, rapidly parasiticidal activity with limited cross resistance with other antimalarial medications (Haldar et al., 2018). The mechanism of action of all artemisinin derivatives is linked to the endoperoxide bridge and is thought to act by releasing free radicals resulting in oxidative stress in the parasite following the cleavage of the endoperoxide bridge, and through interaction with the haem present in the parasite (Katzung, 2004; Rosenthal, 2021.). The artemisinin derivatives may also inhibit parasite growth by inhibiting glutathione S-transferase, an enzyme involved in the breakdown of cytotoxic haematin in the parasite (DrugBank, 2021b; O'Neill et al., 2010). The derivatives kill all forms of parasites in an erythrocytic stage of *Plasmodium* parasites, but it is active against the liver forms of the parasite development and gametocytes (Wilson et al., 2013).

Artemisinin derivatives are currently the most potent and widely used antimalarial chemotherapeutic agents (Heller and Roepe, 2019). The main artemisinin derivatives include: dihydroartemisinin, artesunate, arteether, artemether and artemoil (Figure 1.6)**,** and are used either as monotherapy or as artemisinin-based-combination therapy (ACT) in the treatment of a multidrug-resistant *P. falciparum* malaria (Heller and Roepe, 2019).

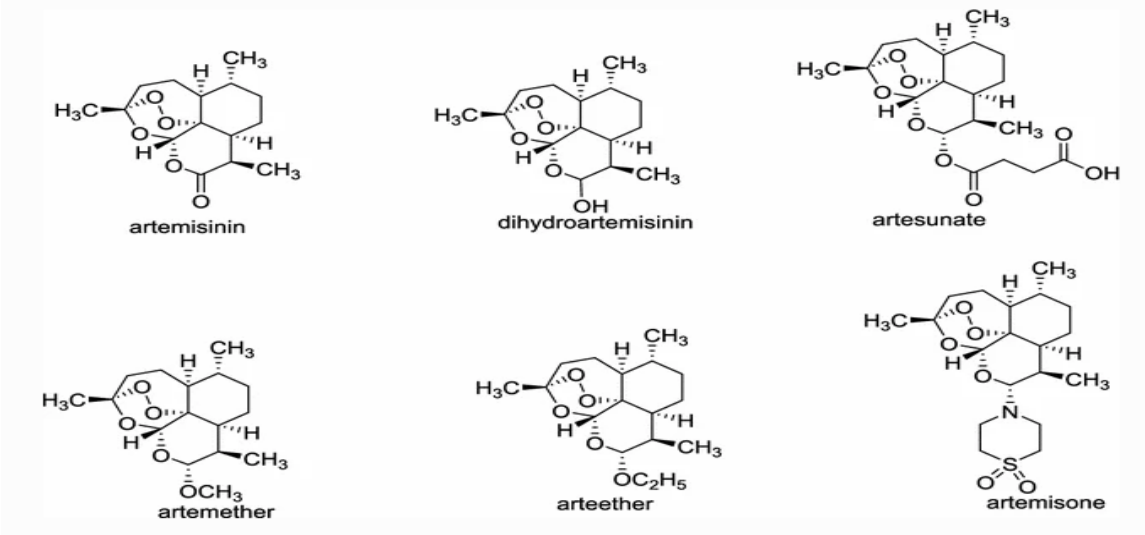


Figure 1.6: Structure of artemisinin and derivatives (Zhang et al., 2018).

1.8.4.1 Pharmacology of artesunate

Artesunate is the hemi-succinate ester of dihydroartemisin (Figure 1.5) and the most potent of all currently known artemisinin derivatives (Kouakou et al., 2019). Artesunate is used either as monotherapy for the treatment of severe malaria or in ACT with a partner drug for the treatment of an uncomplicated malaria, such as artemether-lumefantrine (Kouakou et al., 2019).

Artesunate has a very short elimination half- life, it is estimated to be eliminated in less than five minutes following the intravenous administration (DrugBank, 2021b). Its active metabolite dihydroartemisinin is eliminated within an approximate period of 1 to 2hours (Talman et al., 2019). Artesunate is a well-tolerated drug with commonly encountered side effects including anorexia, nausea, vomiting, and dizziness. However, some serious side effects such as, reduced reticulocytes count, anaemia, eosinophilia, elevated AST, neutropenia, and transient ECG abnormalities have been rarely reported (SADOH, 2019b).

1.8.4.2 Pharmacology of artemether - lumefantrine

Artemether-lumefantrine is a fixed dose ACT combination that is effectively used in South Africa for the treatment of uncomplicated malaria (SADOH, 2019). Artemether, the methyl ether derivative of dihydroartemisinin, is rapidly metabolized into its active metabolite alpha-dihydroartemisinin (DrugBank, 2021a). Artemether has a rapid onset of action which result in a rapid clinical improvement of the patient condition, by

reducing the number of erythrocytic malaria parasites in the blood (Rosenthal, 2021). However, due to its rapid eliminated from the body, it is co-administered with the longer acting lumefantrine to clear residual parasites and delaying the onset of resistance (SADOH, 2019; Rosenthal, 2021).

Lumefantrine is a highly lipophilic with an octanol: water petition co-efficient (log P) of 8.34 that delays its absorption with a lag time of 2 hours and 18 hours for a complete absorption (Huang et al., 2012). The lumefantrine was found to be highly lipophilc in a research that investigated the physiochemical properties of lumefantrine (Babalola, 2013). However, its absorption is improved when taken with fatty foods, and has a 99.7% plasma protein binding capacity in the human blood with an elimination half-life of 3-6 days (Huang et al., 2012, 2018; Rosenthal, 2021).

Both artemether and lumefantrine are metabolized by cytochromes P450 (CYPs) enzymes, viz: CYP2B6 and CYP3A4 for artemether, and CYP3A4 for lumefantrine (Navaratnam et al., 2000). Hence, the pharmacologic properties of these drugs can be altered by CYP enzymes inhibitors or inducers (Navaratnam et al., 2000; Huang et al., 2012). Artemether-lumefantrine (Coartem™) is well tolerated with commonly reported side effect including headache, dizziness, abdominal pain, cough, myalgia, palpitation, fatigue, sleep disturbances and asthma (Ntamba et al., 2019; SADOH, 2019).

1.8.4.3 Artemisinin resistance: delaying a malaria-free world

Artemisinin resistance is defined as “delayed parasites clearance from the blood stream of a malaria infected patient treated with an ACT” (WHO, 2019c). However, this delayed clearance is known to affect only the ring stage of the *Plasmodium* parasites, as such it is more accurately defined delayed clearance as “partial resistance” (WHO, 2019c); with resistance to the partner drug characterised by a late clinical or a late parasitological failure (Slater et al., 2016).

Antimalarial drug resistance can seriously weaken the effectiveness of chemotherapy, cause malaria resurgence, and derail or reverse any malaria elimination campaign with the goal of having a malaria-free world (WHO, 2019; Siddiqui et al., 2021). A malaria-free world is one of the important visions of the global technical strategy for malaria elimination 2016-2030, which includes the aim to have at least ten countries free of malaria by the year 2020 (Yeung, 2018; WHO, 2019a).

The malaria parasite is resistant to all the currently used antimalarial agents with resistance developing to artemisinin over the past decade (Rosenthal, 2021). The artemisinin resistance was initially reported in the western Cambodian border, with six countries of Greater Mekong Sub-region (namely, Cambodia, Thailand, Loa PDR, Myanmar, China, and Vietnam) reporting confirmed artemisinin resistance mutations (WHO, 2018a), but is now spreading to other countries (Noedl et al., 2008; Siddiqui et al., 2021). The report of an emerging artemisinin resistance in WHO African sub-region is alarming, because it could lead to a devastating impact on the malaria morbidity and mortality (WHO, 2021). An estimated additional 78 million cases of malaria, that is 7% increase in a situation without any resistance were expected, if artemisinin and partner drug resistance spread in Africa, at a level like what is currently seen in Cambodia (Slater et al., 2016).

1.9 Knowledge, Attitude and Practise in the Management of Malaria

Understanding of the community knowledge, attitudes and practices is essential to reduce the burden of malaria (Kinung'hi et al., 2010; Uma et al., 2016). It is generally well known that reducing the number of mosquito breeding sites, which is accomplished through environmental management and control, stands as the ideal method for control of mosquito borne diseases (Mehta et al., 2015). Attaining good environmental control requires community motivation which can be achieved through health education ((Mehta et al., 2015). In addition to the environmental control, the use of LLINS and mosquito repellent are known to protect an individual from mosquito bites (Pell et al., 2019). Community participation is essential for the development of a suitable, sustainable, and effective malaria control program (Pell et al., 2019). To achieve this, it is important to assess and understand the level of education of the target population, their attitude and practices towards malaria (Mehta et al., 2015). Furthermore, malaria-related knowledge, attitude and preventive practices has been reported to varies between the individuals living in malaria non-endemic and those living in malaria endemic areas (van Benthem et al., 2006). Hence, with this in mind it was decided to conduct a comparative study on malaria-related knowledge between South Africa and Nigeria.

1.10 Aims and Objectives of the Study

1.10.1 Aims

The aims of this study were to assess and compare the malaria-related knowledge and preventive measures in South Africa and Nigeria and to assess the in vitro efficacy of some of the mosquito' repellents being used by the public in Johannesburg, South Africa.

1.10.2 Objectives

The objectives of this study were:

1. To assess and compare malaria-related knowledge, attitudes, and preventative practises of the participants in Johannesburg (South Africa) and Birnin Kebbi Metropolis (Nigeria).
2. To assess and compare the knowledge of HCPs in South Africa and Nigeria on the management of malaria.
3. To determine if clinical experience influences the choice of medications for the management of malaria by the HCPs and if the current South African and Nigerian malaria treatment and prevention guidelines are adhered to.
4. To determine and compare the most common side effects associated with the use of antimalarial medications and mosquito repellents in South Africa and Nigeria.
5. To collate a list of the more commonly used spatial mosquito repellents used by the public, students, and HCPs in Johannesburg.
6. To evaluate the in vitro efficacy of fifteen most used mosquito repellents reported by the respondents in Johannesburg.

CHAPTER TWO:
RESEARCH METHODOLOGY

This study was divided in to two parts. Part one is a descriptive cross-sectional study which was carried out at three public hospitals in Johannesburg, South Africa and two public hospitals in Birnin Kebbi Metropolis, Nigeria. This study was also carried out at the faculty of health sciences of the University of the Witwatersrand, South Africa, and College of Health Sciences, Federal university Birnin Kebbi, Nigeria. The second part of this study was laboratory based and involved the evaluation of the efficacy of fifteen commercially available mosquito repellents in Johannesburg South Africa.

2.2 Study Sites and Population Cohort

Part one of this study was carried out in five hospitals. Three were in South Africa located in Johannesburg, South Africa, while two were in Nigeria, located in Birnin Kebbi Metropolis, Kebbi State, North-western area of Nigeria.

2.2.1 Johannesburg city in South Africa.

Johannesburg is the largest city in South Africa, and it is among the 50 biggest cities in the world with a total population of 5,782,747, and an estimated annual growth rate of 3.01%. Most of its population can read and write with a literacy level of 98.7%.

Johannesburg has a total surface area of 334,81 square kilometres located within the Gauteng province (Makhubu, 2016; WorldPopulationReview, 2020). It is malaria-free and located within the Gauteng province. However, malaria cases are often reported in Johannesburg or Pretoria and are mainly classified as imported cases (SADOH, 2019b). In addition to this, some malaria cases cannot be associated with a travel history, and these will then be classified as a “local case”. Case investigations generally identify these cases as “odyssean” malaria (SADOH, 2019b). For example, in mid-February 2017 there was a report of possible odyssean transmission of malaria within the province, when two confirmed cases were reported at Doornpoort, Pretoria, Gauteng. The patients did not have any history of travel to the endemic areas (CDC, 2017).

Data collection for the first part of this study (comparative study) was obtained from three public hospitals and the University of the Witwatersrand campus (Faculty of

Health Sciences, FHS) in Johannesburg. The selection of the hospital study sites was based on the multistage sampling methods, firstly the number of all the health facilities in the city of Johannesburg was obtained from the census 2004. Eight public and 2 specialist hospitals were listed in the city of Johannesburg (Census, 2004). Three public hospitals, namely the Charlotte Maxeke, Chris Hani Baragwanath and Helen Joseph Hospitals, were selected according to the bed capacities. The study participants were selected from these hospitals by using convenient sampling method. These three hospitals provide training for students registered at the Faculty of Health Sciences, University of the Witwatersrand, and are located within the city of Johannesburg.

The FHS at the University of the Witwatersrand teaches both undergraduate and postgraduate students, and in 2019 there was a total number of registered undergraduate and postgraduate students of 3,381 and 2,539, respectively. Below is a short description of the hospitals included in the study:

2.2.1.1 Charlotte Maxeke Johannesburg Academic Hospital

The first teaching hospital, namely the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) is located at 17 Jubilee Road, Parktown, Johannesburg. The hospital has a bed capacity of 1,088 beds with more than 4,000 support and professional staff members (TIPS, 2002a) (Figure 2.1 A).

2.2.1.2 Chris Hani Baragwanath Academic Hospital

The Chris Hani Baragwanath Academic Hospital (CHBAH) is the world's third largest hospital and located in Soweto, at 26 Chris Hani Road, Johannesburg, South Africa. It has a bed capacity of approximately 3,200, with about 6,760 staff members (Hospital, 2010) (Figure 2.1 B).

2.2.1.3 Helen Joseph Hospital

The Helen Joseph Hospital is in Auckland Park, Johannesburg, South Africa; prior to 1997 it was called J.G Strijdom Hospital named after the 5th prime minister of South Africa, Johannes Gerhardus Strijdom (Hospital, 2021). The hospital has a total of 1,886 staff, which including 878 nurses, 220 doctors and 788 support staff, with a bed capacity of 512 (TIPS, 2002b; Census, 2004) (Figure 2.1 C).

Figure 2.1: Locations of the three study hospitals in South Africa.
Where A: Charlotte Maxeke Johannesburg Academic Hospital (GOOGLEMAP, 2022a, B: Chris-Hani Hospital (GOOGLEMAP, 2022b) and C: Helen Joseph Hospital (GOOGLEMAP, 2022d).

2.2.2 Birnin Kebbi Metropolis in Nigeria

The geographical location of Nigeria makes its climate suitable for malaria transmission in all the six geopolitical zones of the country. The climate is tropical with a dry season occurring between October to March, while the wet season occurs between April to September, such that the temperature oscillates between 25 to 45°C (FMOH, 2013).

Birnin Kebbi is a city located in the Northwest geopolitical zone of Nigeria with a population of 125,000 people and is the capital of Kebbi State. It is one of the 36 states in the country. and is located at the coordinates of latitudes 12.466078 and a longitude of 4.199524. The people of Birnin Kebbi are mainly Muslims with farming stand as their main business, with an annual rainfall of 787.53 ± 24.03mm (Ismail and Oke, 2012).

2.2.2.1 Federal Medical Centre

The Federal Medical Centre (FMC), Birnin Kebbi (BK) is the biggest hospital in Kebbi State and is located along the Dukku Barack Road, in Birnin Kebbi, the capital of Kebbi State, Nigeria (Kebbi, 2022) (Figure 2.2 A). It has a total of 300 bed capacity and a total staff population of 1,783. It provides tertiary health care services to the people of the Kebbi State and the neighbouring states, as well as some patients from the neighbouring country like the Niger Republic.

2.2.2.2 Sir Yahya Memorial Hospital

The Sir Yahya Memorial hospital (SYMH) is the 2nd biggest tertiary hospital in Kebbi State, with a total of 840 staffs and is located along the Haliru Abdu, Road, Birnin Kebbi, Nigeria (PlatTechnologies, 2020). The FMC and SYMH hospitals are the two main tertiary hospitals in the Kebbi state serving as the main referral centres. The FMC is being operated by the federal government, while the SYMH is operated by the Kebbi state government and these hospitals serve a population of over 4 million people (Olaosebikan et al., 2020) (Figure 2.2 B).

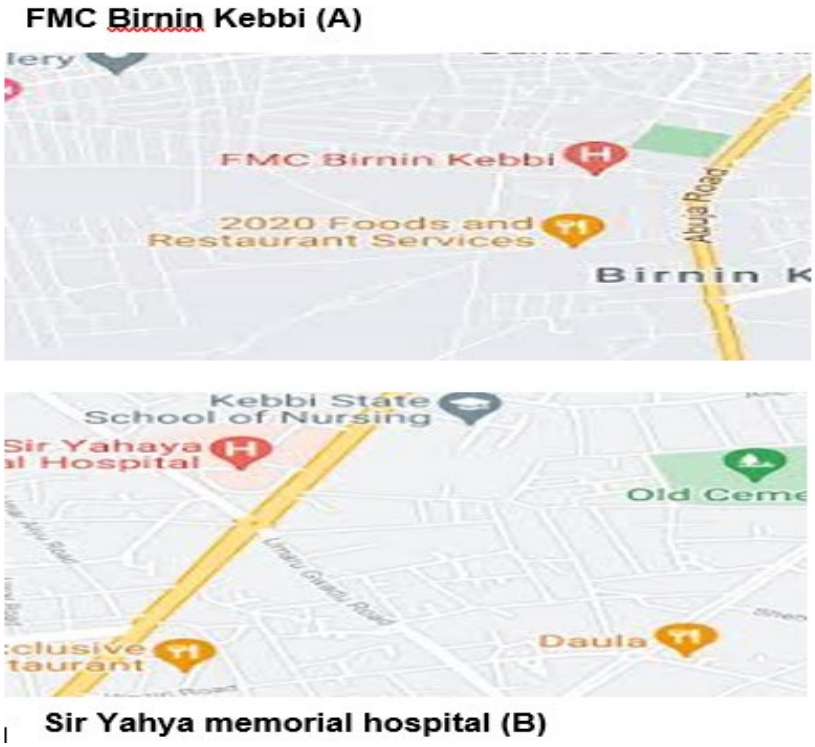


Figure 2.2: Locations of the two study hospitals in Nigeria.
Where: A: Federal medical centre Birnin Kebbi (GOOGLEMAP, 2022c) and B : Sir Yahya Memorial Hospital Birnin Kebbi (GOOGLEMAP, 2022e).

2.3 Study Design

The descriptive cross-sectional study of Part one included a semi-structured self-administered questionnaire. A major part of the questionnaire for this study was developed from the previously published study by Padonou et al. (2018). Approval to use and modify the instrument was sort from the corresponding author Dr Germain Gil Padonou, University of Abomey Calavi, Benin Republic (Appendix A). The context validity of the questionnaire instrument was confirmed by a group of experts including both doctors and nurses at the University of the Witwatersrand, South Africa. .

There were four sections in this instrument, with a total of 58 variables and Cronbach's alpha of 0.86 (Appendix B).

1. Section 1: Demographic information: This section consists of 10 items through which the information on age, gender, occupation, duration of experience, highest level of education and academic level of the participants were obtained.
2. Section 2: Knowledge on malaria symptoms and transmission: This section consists of 10 items and in this part the respondent's basic knowledge on the cause, transmission, signs and symptoms of malaria were obtained.
3. Section 3: Knowledge on malaria management: This section is mainly for HCPs and there were 21 items which were used to assess the HCPs knowledge and preference on the management of malaria according to the South African protocol.
4. Section 4: Attitudes and perceptions regarding malaria: This consisted of 17 items used to assess the attitudes and perceptions of the respondents on malaria and its management.

2.4 Study Population and Sample Size Determination

The total populations from the study sites in South Africa were 18,742, comprising of 6,936 from CHBAH, 4,000 from CMJAH, 1,886 from Helen Joseph Hospital and 5,920 from the University of the Witwatersrand FHS students, University of the Witwatersrand. While in Nigeria, the study sites have a total population of 2,946 which consisted of 1,783 FMC, Birnin Kebbi, 840 from SYMH and 323 students from the College of Health Sciences, Federal University, Birnin Kebbi.

As determined by the Raosoft calculator (http://www.raosoft.com/samplesize.html) and with the assistance of WITS statistician, the sample size was estimated to be 377 and 340 participants with estimated populations of <20,000 and 2,946 in South Africa and Nigeria, respectively. All the sample sizes were calculated at 95% confidence interval (CI) and 5% margin of error. An attrition of 5.8% and 15.0% were added to the South Africa and Nigeria calculated sample sizes, which resulted in a total sample size of 400 participants, from each country to be enrolled into the study. The 400 questionnaires were shared between the study sites by using a sampling method proportional to size (Table 2.1).

Table 2.1: The distributions of the sample size between the study sites using a sampling method proportional to the size (South Africa and Nigeria).

Study site	Population	Percentage (%)	Questionnaires (N)
South Africa			
CHBAH	6,936	37	148
CMJAH	4,000	21.3	85
Helen Joseph	1,886	10.1	40
WITS FHS Students	5,920	31.6	127
Total	18,742	100	400
Nigeria			
FMC B/K	1,783	60.5	242
SYMH	840	28.5	114
FUBK CHS students	323	11.0	44
Total:	2,946	100	400

2.5 Sources of Data, Inclusion and Exclusion Criteria

Approvals were obtained from the Head of the Departments at the different study sites prior to the onset of the study. The HCPs were approached individually or at the end/beginning of their clinical meetings held mainly on Friday and requested to participate voluntarily in the study by completing the consent form (Appendix C). Similarly, the study participants from the public, including patient relatives, visitors, and outpatients, were approached individually within the wards and around the hospital

premises Only those participants that voluntarily completed the consent forms were included in the study.

The instrument was sent to the FHS students at the University of the Witwatersrand in South Africa and College of Health Sciences Students of the Federal University Birnin Kebbi, in Nigeria through their various email addresses and their WhatsApp groups.

The return from the Emails and WhatsApp was very low from both countries, as such they were also approached with hard copies usually before the beginning of their lectures and given a brief presentation about the research and asked to complete the survey instrument at their own convenience for those that voluntarily wished to partake in the study by completing the consent form. The effects of COVID-2 lock down and alteration in education format severely affected the response rate by healthcare professions who were inundated with patients and students who were overwhelmed with the new on-line format of learning.

The questionnaire was captured into the Research Electronic Data Capture (REDCap) database of the University of Witwatersrand, and it was either supplied as an electronic or hard copy to the participants. The data collections were performed between November 2019 to November 2021.

2.5.1 Inclusion criteria

For the Part one of the study, the inclusion criteria were, all the HCPs, out-patients, accompanying hospital visitors in the selected hospitals, and FHS students over the age of 18 years that agreed to participate in the study.

2.5.2 Exclusion criteria

The exclusion criteria for Part one of the study included those who refused to sign the consent form and aged less than 18 years. Those aged less than 18 years were excluded, because in South Africa and Nigeria before a person turned 18 years is considered to be a child; hence they do not attain the legal consent for procedures involved in research (Alake, 2020; LegalAidSouthAfrica, 2022).

2.5.3 Data Management and Statistical Analysis

The completed questionnaires were entered into the REDCap at a regular basis, often daily after returning from the hospitals, thereafter the data was then downloaded for

cleaning, cross checked for completeness, and imported into the IBM Statistical Package for the Social Sciences (SPSS) version 27.0 for analysis.

The demographic information was analysed using descriptive statistics, mean and standard deviation were reported where the data was found to be normally distributed using Shapiro wilk test and histogram. In a situation where it is not normally distributed median and interquartile range were reported. Some categorical data were presented in graphs, mainly simple bar chart, clustered bar chart and pie chart.

Cross tabulations were performed between the categorical variables using a Pearson Chi-square test, while odd ratio was used to compare the outcomes of some variables obtained from the participants living in Nigeria, which is malaria endemic country (exposed) with the outcomes obtained from the participants living in Johannesburg, South Africa, which is malaria-free area (non-exposed) as this statistics can be performed in cross sectional studies (Szumilas, 2010). All the statistically significant associations were reported at a p value <0.05 and 95% CI.

The participants malaria-related knowledge was computed by assessing the ability of the participants to correctly identified six malaria knowledge domains viz: common malaria symptoms, mode of transmission of malaria, season with highest malaria transmission, preventive strategies, breeding site and malaria as a cause of anaemia (Table 2.2). The knowledge was categorised as good versus poor.

Table 2.2: Malaria-related knowledge domains scores (personal communication, Wits its Statistician).

Characteristics	Score
Common Malaria Symptoms	
Fever	1
Chills	1
Headache	1
Joint pains	1
Nausea and vomiting	1
Abdominal pain	1
Convulsions	1
Mode of transmission of malaria	
Infected female *Anopheles* mosquito bites	1
Season with highest malaria transmission	
Rainy Season	1
Preventive Strategies	
LLINs	1
IRS	1
Health promotion	1

Case management	1
Larval Source management	1
Breeding Site	
Standing Water or Garbage	1
Can Malaria cause anaemia?	
Yes	1
Total	16

The minimum and highest scores obtainable were 0 and 16 respectively, those with a score of ≥50% (8 and above) was regarded as having good knowledge, while those with a score of ≤50% (0 to 7) was regarded as having poor knowledge (Okafor et al., 2019).

While the participants' attitude and practices on malaria was computed by totalling their scores on the questions that assessed their attitudes and practices towards malaria treatment and prevention. The total score obtainable ranges from 0 to 10, any participants with greater than or equals to ≥50% (≥5/10) of the total score was regarded as having good attitude, while a score less than 50% (0 to 4) of the total score was regarded as having poor attitude (Okafor et al., 2019). (Table 2.3).

Table 2.3: Participant's attitude scoring domains.

Variables	Scores
Do you think malaria is a preventable disease?	
Yes	1
Attitudes on Personal protective measures (Which of these do you think will provide personal protection against malaria?)	
LLINs	1
Mosquito repellents	1
Clean environment	1
Anti-malarial prophylaxis	1
Which of these prophylactic drugs have you ever used?	
Mefloquine	1
Doxycycline	1
Atovaquone-Proguanil	1
Treatment seeking behaviours?	
Within 24 hours	1
Do you always complete drugs as prescribed?	
Yes	1
Total	10

2.6 Part Two

In preparation for the Part 2 laboratory-based study in which the efficacy of fifteen commercially available mosquito repellents were evaluated, a collation of mosquito repellents was prepared.

2.6.1 Repellent information

Information with regards to commercially available mosquito repellents was obtained through the market survey conducted by checking at the pharmacies in the mall, street stalls, warehouses, and supermarkets within Johannesburg. In addition, the online mosquito repellent information was obtained through an online search using search terms like: “mosquito repellent in Johannesburg”, “insecticide in Johannesburg,” “available citronella products in Johannesburg,” “synthetic mosquito repellents in Johannesburg” “DEET product in Johannesburg,” “natural mosquito repellent in Johannesburg” and many others. The information was collated and the available information such as composition, instructions of use, registration with South African Bureau of Standards (SABS) was documented. The 15 mosquito repellents products evaluated were purchased from Dis-Chem, at the Mayfair Station and Clicks pharmacies in Johannesburg (Table 2.4). The repellent efficacy testing was performed at the WRIM laboratories using a non-contact method with a two-sided plastic netted chamber constructed according to WHO efficacy assay guideline (WHO, 2009).

Table 2.4: List of 15 repellent products tested.

No	Name Of the Products	Formulations
1	Tabard.	Lotion
2	Citro-Bar Soap.	Soap
3	Life Trek, Mosquito Spray.	Spray
4	Medi Scabiol Soap.	Soap
5	Mosquito Guard.	Lotion
6	Anti-Mozzie Camping, Outdoor and Indoor Cream.	Cream
7	No-Squito Lotion.	Lotion
8	Pure Begining Organic Care, 100% Natural Insect Repellents.	Spray
9	Medic Insect Repellent Cream.	Cream
10	All-Natural Guard Insect Repellent.	Lotion
11	So Pure Naturally, Mosquito Spray.	Spray
12	Moz-Free Mosquito Repellent.	Cream
13	Mylol Perfumed Mosquito Repellent.	Stick
14	Mosquito Patch Insect Repellents.	Patch
15	Bennets, Mozzie Stick.	Stick

2.6.2 Repellent Assay - Biological material

The Congo *Anopheles gambiae s.s.* (previously called S- molecular form) (COGS colony) housed at the WITS Research Institute for Malaria (WRIM) Maureen Coetzee Insectary was used for assays (Koekemoer et al., 2011). Insectary rearing conditions for the colony were standardised at a temperature of 27 ± 2°C, relative humidity of 80 ± 10% and photoperiod of 12 hours light to 12 hours dark. Twenty actively host seeking, female *Anopheles* mosquitoes were starved for 12 hours and used per volunteer throughout the experiment, making a total of 80 females *Anopheles* mosquitoes for the four volunteers used per each repellent evaluated. The age of the mosquitoes used for each repellent product for the repellency assay **(Table 2.5).**

Table 2.5: Repellent products tested, and age of the mosquitoes used.

Repellent product tested	Age (days)
Tabard	6
Citro-bar Soap	6
Life Trek, Mosquito Spray	7
Medi Scabiol Soap	6
Mosquito guard	7
Anti-mozzie camping, outdoor / indoor cream	5
No-squito lotion	6
Pure Begining Organic Care.	6
Medic Insect Repellent Cream	6
All-natural guard insect repellent	7
So Pure Naturally, Mosquito Spray.	6
Moz-Free Mosquito Repellent	7
Mylol perfumed mosquito repellent	7
Mosquito Patch Insect Repellents	7
Bennets, Mozzie stick	6
	Median 6.0 IQR = 6.0-7.0)

2.6.3 Evaluation of repellents efficacy

The assays were conducted weekly on Friday mornings when adult mosquitoes were available from the insectary, with the following steps undertaken to evaluate the repellent effect of the test products (Figure 2.3):

1. Four volunteers were used for each repellent product throughout the experiment (resulting in a total of four replicates) as per WHO guidelines (WHO, 2013). Four volunteers were used for each repellent to control for any inherent variables associated with using one volunteer. This could be due to the differences in olfactory characteristics, dermal structure, and innate repellence; such that each volunteer act as their own control, and this will also help to determine the population dynamics affecting the efficacy of the repellents (Mukabana, 2002).
2. A week before the assay, the volunteers completed a short questionnaire to assess their previous history of allergy and those with a positive history was excluded from conducting the experiment (Appendix D).

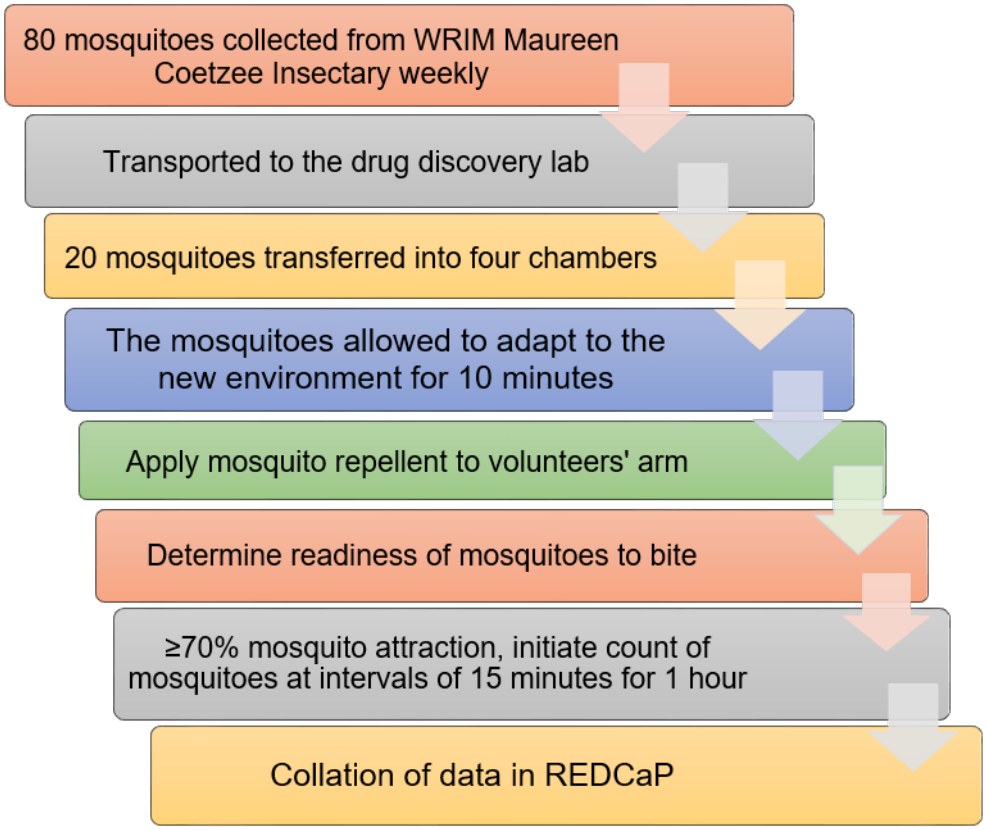


Figure 2.3: The repellent efficacy assay procedure.

3. A day before the onset of the assays the volunteers were invited to the WRIM unit on the tenth floor of the FHS Building to become familiar with the SOP of the experiment and to sign the consent form (Appendix D). At that time the repellent product to be tested was applied to a small area on their arm to look for any potential allergic reaction the next day. The volunteers were instructed not to apply any perfume, aftershave, or aromatic lotion the morning of the experiment to avoid interference with the potential repellent properties of the test compound.
4. Twenty female *Anopheles gambiae s.s* were collected from the Maureen Coetzee *Malaria Insectary* and transferred into the dual choice chamber using an aspirator in an environment with the optimal temperature and humidity (Figure 2.4).

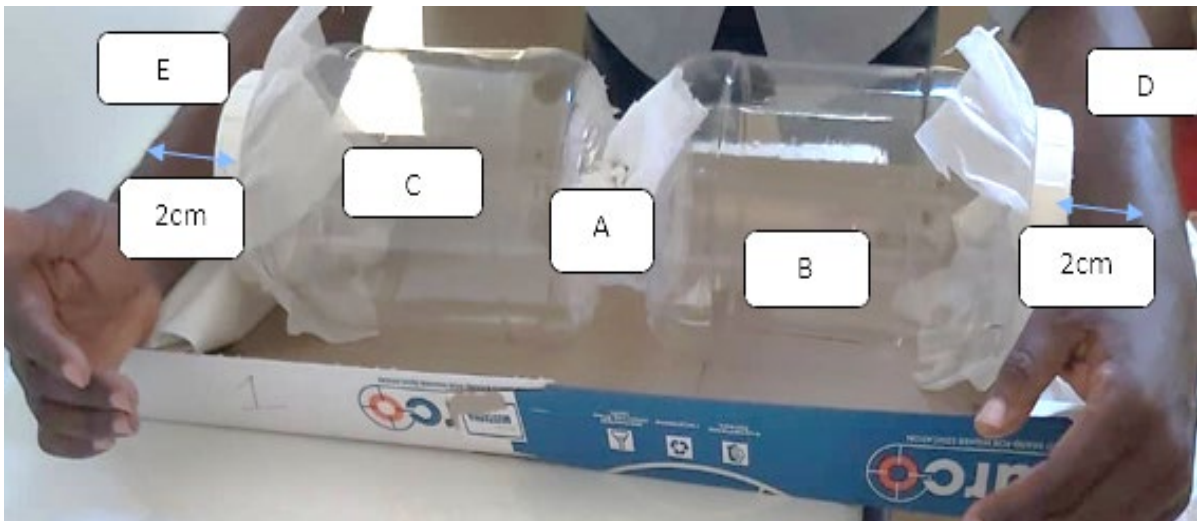


Figure 2.4: Mosquito repellency Plastic-Neted-Dual Choice Test Chamber.
Mosquitoes were placed into the device (chamber A). Mosquitoes were allowed to freely migrate between the test (B) or control (C) chambers. D and E illustrate the volunteers right (Test) and left (Control) arms placed 2cm away from the net.

5. The repellent to be tested on that day was then applied on the volunteer's anterior aspect of the right arm (test arm), using a measuring instrument of 17cm X8.5cm to ensure equal surface area of application for all the participants **(**Figure 2.5**),** while the left arm served as control. All the applications were done according to the manufacturer's instructions.
6. Before the commencement of all the assays, the readiness of the mosquitoes to bite were always tested with the control arm, if <70% attraction rate was noted the assays was canceled and rescheduled to another week. If >70% attraction rate was noted both arms were then placed at the side of the chambers, 2cm away from the nets.

All the assays were conducted for a duration of one hour and the mosquitoes attracted to the nets and those that stayed in the chambers were counted at the 15 minutes interval and recorded in the data collection sheet (Appendix E). The moribund mosquitoes were only counted at the end of the procedure. The moribund mosquitoes were any mosquito that could not stand (e.g., has 1 or 2 legs); any mosquito that could not fly in a coordinated manner; a mosquito that was its back, moving its legs and wings, but unable to take off; and a mosquito that could stand and take off briefly, but fell down immediately (WHO, 2013). Only one product was tested per day.

Figure 2.5: A measure template of 17cm x 8.5cm that was used to apply the test repellents for all the participants.

7. At the end of the procedure, the plastic chambers were then cleaned with 70% alcohol, rinsed with water, and allow to air dry for used the following week.
8. The data obtained was then immediately transferred into REDCap and was used to calculate the protection rate, percentage attraction, percentage responding and spatial activity index according to WHO guidelines (WHO, 2013).
9. The percentage attraction of the tested repellents products was calculated using (Equation 2.1), which is the determinant of the spatial repellence activity of any insect repellent product, good repellence activity is indicated by a lower percentage attraction, it is calculated by dividing the average number of mosquitoes counted at the treated arm net divided by the total number of mosquitoes used for the test, minus any damaged mosquito (WHO, 2013). The average number of the mosquitoes on the treated arm net was obtained by calculating the mean of the number of mosquitoes counted on the treated arm net over an hour at interval of 15 minutes and for all the four volunteers (Equation 2.2).

$$\text{Percentage attraction } (\%) = \frac{\text{Average number of mosquitoes on treated arm net}}{\text{Total number of mosquitoes used } (20)} * 100$$

Equation 2.1: Formula used to calculate the percentage attraction of the repellent products tested (Mitra et al., 2019).

$$\text{Average number of mosquitoes on treated arm net} = \frac{\text{Total number of mosquitoes counted in all the four assays}}{4}$$

Equation 2.2: Formula used to calculate the Average number of mosquitoes on the treated arm net of the repellent products tested.

10. While the percentage repellency, which represent the efficacy of the tested repellents was obtained by using (Equation 2.3) which compared the average number of mosquitoes that landed or attempted to bite at the treatment and control arm net (Naucke et al., 2007; Lupi et al., 2013).

$$\text{Percentage repellency } (\%) = (\mathrm{C} * \mathrm{t} - \mathrm{T})/(\mathrm{C} * \mathrm{t})\mathrm{x}100.$$

Equation 2.3: Formula used to calculate the percentage repellency of the repellent products tested. Where C stand for the average number of mosquitoes counted in the control chambers, T stand for the average number of mosquitoes counted in the treatment chambers, t stand for the duration of time used for the assay which is 60 minutes in this study.

11. The spatial repellency of the repellents products was calculated using the spatial activity index (SAI), which is defined as the proportion of mosquitoes prevented from entering the treatment chamber in relation to the total number of the mosquitoes moving within the system (Equation 2.4) (WHO, 2013).

$$\mathrm{SAI} = \left[\frac{\mathrm{NCAC}-\mathrm{NTAC}}{\mathrm{NCAC}+\mathrm{NTAC}}\right] \times \left(\frac{\mathrm{TNCT}}{\mathrm{N}}\right)$$

Equation 2.4: Equation used to calculate the spatial activity index of the tested repellent products. Where NCAC=number of mosquitoes in the control arm chamber, NTAC = number of mosquitoes in the treated arm chamber, TNCT= total number of mosquitoes in both control and treated arm charm chamber and N = of mosquitoes used for the experiment. $\left(\frac{\mathrm{TNCT}}{\mathrm{N}}\right)$ is also called percentage responding.

2.6.1 Inclusion criteria

The inclusion criteria were lack of any history of an allergic reaction, returned completed standard operating procedure (SOP) and consent forms, negative skin test conducted a day before the experiments and being older than 18 years.

2.6.2 Exclusion criteria

The exclusion criteria were having any form of an allergic reactions, refusal to sign the consent form or SOP, positive skin test conducted a day before the experiment and being younger than 18 years.

2.6.3 Data Management and Statistical Analysis

For the Part two of the study, the data obtained from the mosquito repellent (part two) assays, the protection rate, percentage attraction, percentage responding, and spatial activity index were captured into REDCap, before being downloaded and imported into SPSS version 27.0 for cleaning and analysis.

The percentage mean repellency of the tested repellents was calculated and transformed for comparisons between the mean protections of the control (Tabard^{TM}) and the other tested repellents using ANOVA, the normality of the data was checked (using normogram and shapiro wilk test). Levene test was also conducted to determine the homogeneity of the variance. In a case of a statistically significant non-homogeneity of the variance or an unequal sample size, Welch test were reported.

A *post-hoc* test was also conducted using Turkey's honestly significant difference test (Turkey HSD) to identify the point of statistically significant difference between the means of the control and other tested mosquito repellents.

2.7 Permissions to Conduct the Study

This study was approved by the School of Therapeutic Sciences Protocol Assessment Committee of the University of the Witwatersrand, South Africa (Appendix F). Permission to conduct the study was obtained from the Chief Executive Officers of all three hospitals in South Africa (Appendix G-I) and two hospitals in Nigeria (Appendix J and K). As well as from the registrar of the University of the Witwatersrand in SA and FUBK in Nigeria (Appendix L and M) and from the Head of the following Schools in the FHS: Anatomical Sciences, Clinical Medicine, Oral Health Sciences, Pathology, Physiology, Public Health, and Therapeutics Sciences (Appendix N to T).

2.8 Ethical Considerations

The ethical clearance to conduct the study was obtained from the Human Research Ethics Committee of the University of the Witwatersrand in South Africa (M190657 and M200177) and from the Kebbi State Ministry of Health in Nigeria and FUBK Ethics Committee in Nigeria (Appendix U and V). To note the change of dissertation and ethics titles were approved by the WITS Faculty of Health Sciences Postgraduate Office and Human Research Ethics Committee (Appendix W)

A waiver was obtained from the WITS Animal Research Ethics Committee for the use of *Anopheles* mosquitoes for the repellent efficacy assays (07-11-2017-O) (Appendix X).

Approval to undertake the study in Gauteng Hospitals was obtained from the Gauteng Health Research Committee with the GP number : GP_201909_005 (Appendix Y).

CHAPTER THREE:

RESULTS

This study consists of a descriptive cross-sectional study which compare the malaria-related knowledge, attitudes, and preventive practices of the participants from South Africa and Nigeria (part one) and a laboratory-based study in which the efficacy of fifteen mosquito repellents products were evaluated (part two). In This chapter the analysis of the result obtained from the cross-sectional study, the market and online surveys and repellents efficacy assays were presented.

3.1 Demographic Characteristics

3.1.1 Gender and level of education

A total of 1,144 questionnaires were voluntarily completed, where (65.7%; n = 752) were from South Africa, and the balance of (34.3%; n = 392) from Nigeria. Most of the respondents were females (57.4%; n = 656), followed by males (42.1%; n = 481) and other gender (0.5%; n = 6). There were more female participants from South Africa (62.1%; n = 466), while males (51.5%; n = 202) were the majority in Nigeria. There was a statistically significant differences in gender between the two countries ($p<0.001$). The other genders were all reported from South Africa (Table 3.1).

Most of the participants (for both countries combined) had a tertiary level of education (76.1%; n = 861), only (0.7%; n = 8) of the participants have primary certificate as their highest level of education, while (1.8%; n = 20) have not attended schools. In both countries, the tertiary level was the highest level of education reported (70.5%; n = 527) and (87.0%; n = 334) from South Africa and Nigeria, respectively. Most of the respondent that did not attend school were from Nigeria (60%; n = 12) compared to (40%; n = 8) from South Africa, with a statistically significant difference on the level of education of the respondents between the two countries ($p < 0.001$).

There was a statistically significant difference between the gender and level of education of the respondents ($p<0.001$), this difference was also significant within the respondents from each country ($p < 0.001$) and ($p = 0.025$) in South Africa and Nigeria, respectively (Table 3.1).

.

Table 3.1: Gender and Level of Education.

Characteristics	South Africa % (n) 65.7 (752)	Nigeria % (n) 34.3 (392)	Total % (n) (n = 1,144)	X^2	df	P value
Gender				24.066	2	<0.001
Males	37.2 (279)	51.5 (202)	42.1 (481)			
Females	62.1 (466)	48.5 (190)	57.4 (656)			
Other gender	0.8 (6)	-	0.5 (6)			
Level of education				54.602	3	<0.001
No schooling	1.1 (8)	3.1 (12)	1.8 (20)			
Primary level	0.8 (6)	0.5 (2)	0.7 (8)			
Secondary level	27.6 (206)	9.4 (36)	21.4 (242)			
Tertiary level	70.5 (527)	87.0 (334)	76.1 (861)			

3.1.2 Age characteristics

The mean age of the study participants was 25.95 ± 8.04 years, there were relatively younger participants from South Africa (mean 24.78 ± 7.47 years) compared to participants from Nigeria (28.35 ± 8.62 years, p< 0.001). When grouped in to three different age categories the age of the most participants were within the age range of 21-40 years 71.1% (n = 746), while the least age group in this study was 41 years and above 5.4% (n = 57). (Figure 3.1).

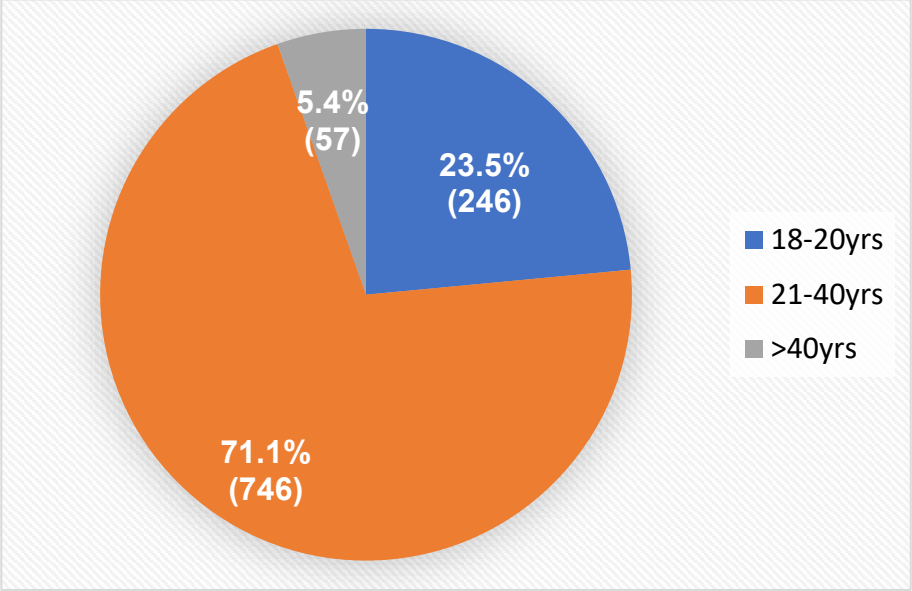


Figure 3.1: The percentage age categories of the study participants.

3.1.3 Occupational status

Of the 1,144 participants, 55.2% (n = 631) were students, 27.5% (n = 315) were HCPs, while 17.3% (n = 198) were public respondents. Majority of the HCPs were nurses 37.1% (n = 117), while the physiotherapist were the least participants among the HCPs 8.6% (n = 27) to respond to the questionnaire (Figure 3.2).

Out of the 631 students, 92.2% (n = 571) were undergraduate, while 7.8% (n = 48) were postgraduate students, where the postgraduate students were all from Wits University South Africa.

Among the 1,144 participants, 36.5% (n = 387) have had a previous history of malaria infection, 1.8% (n = 19) cannot remember their previous malaria history status, while most of the respondents, 61.7% (n = 653), had never experienced a malaria infection. There were significantly higher reported malaria infections among the respondent from Nigeria (98.9%; n = 348) compared to the 5.7% (n = 39) from South. The respondents from Nigeria were more likely to report a previous history of malaria infection compared to their South African counterparts (OR= 1447.77, 95% CI= 513.15-4084.67; p<0.001); however, this finding was already expected as Johannesburg is a malaria-free area compared to Nigeria, which is malaria endemic region (FMOH, 2013; SADOH, 2019b).

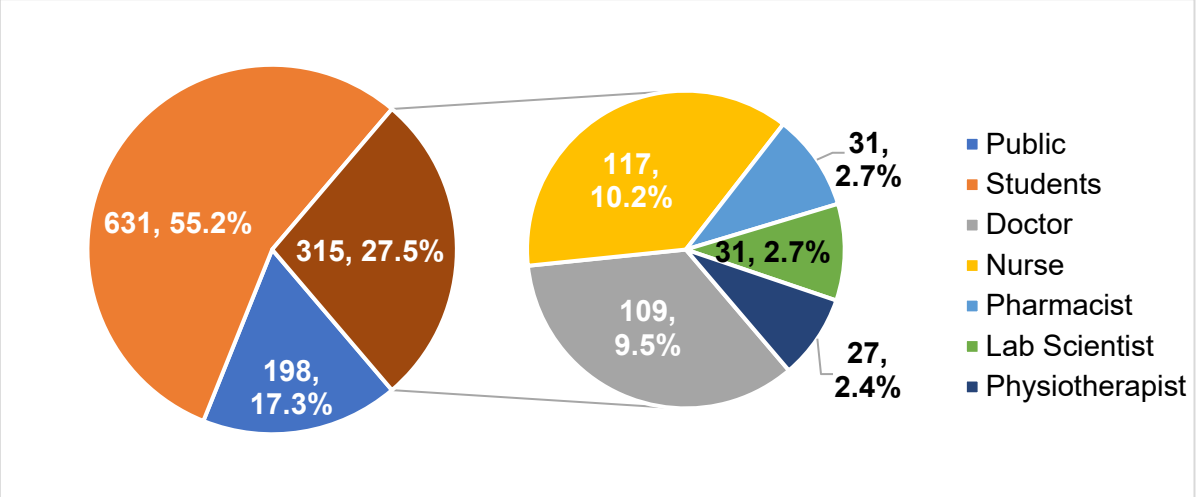


Figure 3.2: Percentage distributions of occupations of the three groups of participants.

Namely Public ( ), Students ( ) and HCPs ( ), including the Doctors ( ), Nurses ( ), Phamacists ( ), Laboratory scientists (and Pysiotherapists ( ) that took part in the Part 1 of the study.

3.1.4 Distribution of HCPs across the study sites

Out of the 315 HPCs that participated in the study, 52.1% (n = 164) were from Nigeria, while 47.9% (n = 151) were from South Africa (P<0.001). Most of the HCPs respondents in Nigeria were from the Federal Medical Centre, Birnin Kebbi (FMC B/K) 75.5% (n = 117), while in South Africa most of the HCPs respondents were from the CMJAH (50.7%; n = 69) (Table 3.2).

Table 3.2: Distributions of HCPs across the study hospitals.

Characteristics	Frequency (n)	Percentage (%)
South Africa	151	47.9
CMJAH	69	50.7
Helen Joseph	36	26.5
CHBH	31	22.8
Nigeria	164	52.1
FMC B/K	117	75.5
Sir Yahya	38	24.5

Note: in this table only 136 out of 151 of the SA HCPs specified their hospitals, also only 155 out of 164 NG HCPs specified hospitals, hence may not add up to 315 HCPs.

3.2 Knowledge on malaria symptoms and transmissions

To better understand the knowledge of the various groups of participants, several questions were posed about malaria symptoms, the malaria vector, transmission, control, and treatment.

3.2.1 Knowledge on malaria symptoms

Seven common symptoms of malaria viz: fever, chills, headache, joint pains, nausea and vomiting, abdominal pain and convulsion were presented to the participants as multiple-choice response question to assess their knowledge on malaria symptoms. Fever was the most known symptom of malaria identified by the study participants (86.3%; n = 987), while the other two most recognised symptoms were headache (68.3%; n = 781) and chills (67.8%; n = 776), the least mentioned of the symptoms was abdominal pain (42.6%; n = 487) (Figure 3.3). Within the groups, 86.7% (n = 273), 90.5% (n = 571) and 72.2% (n = 143) of the HCPs, students and public knew fever as a symptom of malaria, respectively (Figure 3.4).

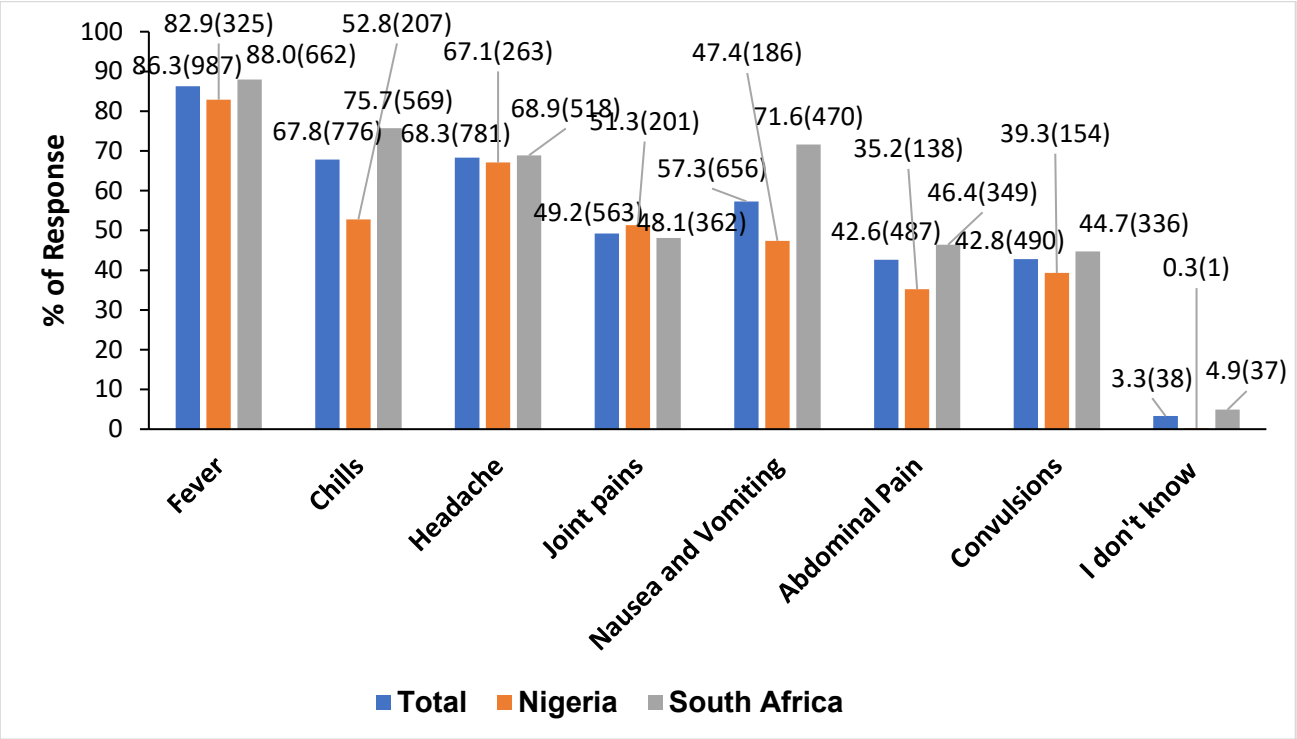


Figure 3.3: Percentage distributions of participants correct responses on Malaria symptoms (Total and study countries).

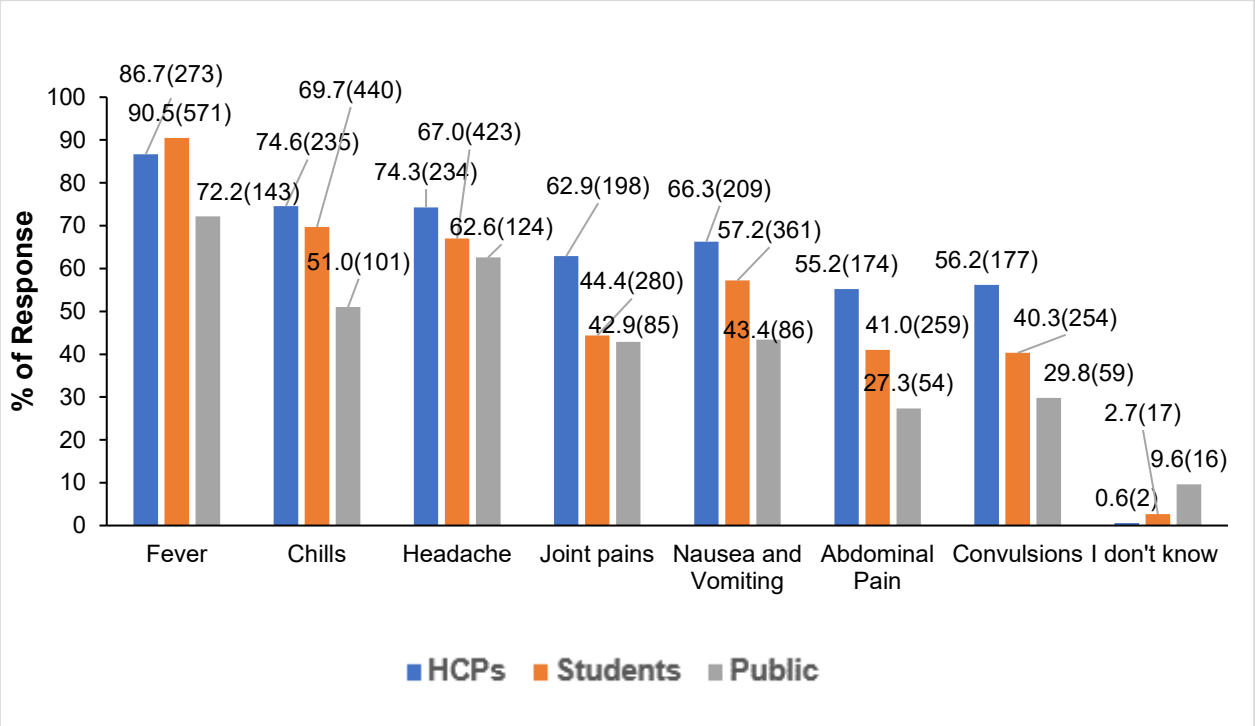


Figure 3.4: Distributions of respondent's knowledge of malaria symptoms based on occupations (total).

The knowledge of the malaria symptoms was statistically significantly different between the study countries on all the seven symptoms with p-values <0.001 for all the symptoms, except for headache (p=0.013). The HCPs and students from South Africa had higher knowledge of malaria-related symptoms compared to the HCPs and students from Nigeria. However, the public respondents from Nigeria had a higher knowledge on malaria-related symptoms compared to the public from South Africa (Figures 3.5, and 3.6).

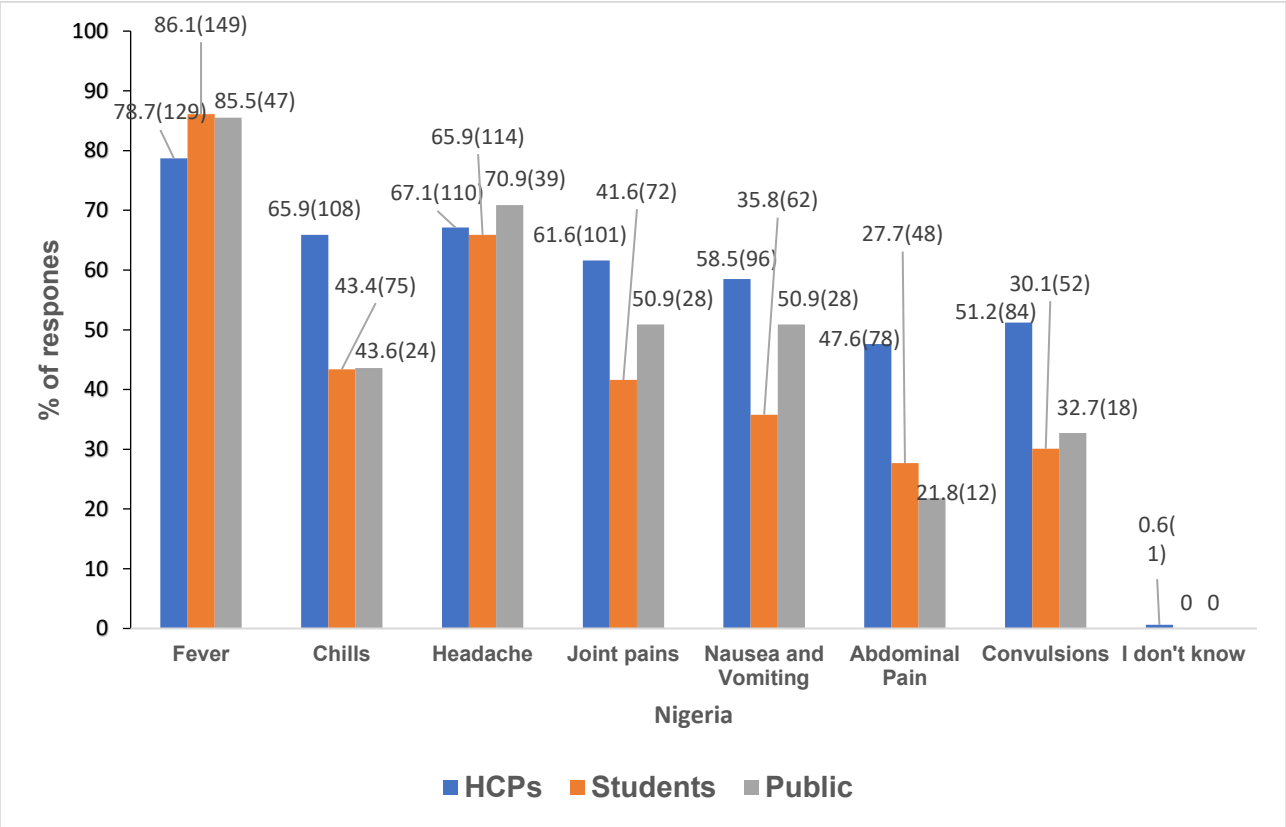


Figure 3.5: Distribution of knowledge of the Nigerian respondents on malaria symptoms based on occupations.

Further analysis revealed that out of the 1,144 participants only 33.8% (n = 387) of the respondents answered all the seven symptoms correctly. There were more participants from South Africa with correct answers for all the symptoms (35.6%; n = 268) compared to 30.4% (n = 119) from Nigeria, although this was not statistically significant different (p = 0.073). Most of the respondents, 99.5% (n = 385) that answered all the symptoms had a good malaria knowledge score compared to 0.5% (n = 2) that answered all the symptoms with poor knowledge score (p < 0.001). The proportion of the HCPs that correctly answered all the seven symptoms were 47.0% (n = 148), which was

statistically higher than the correct responses among the students and public (p<0.001) (Figure 3.7).

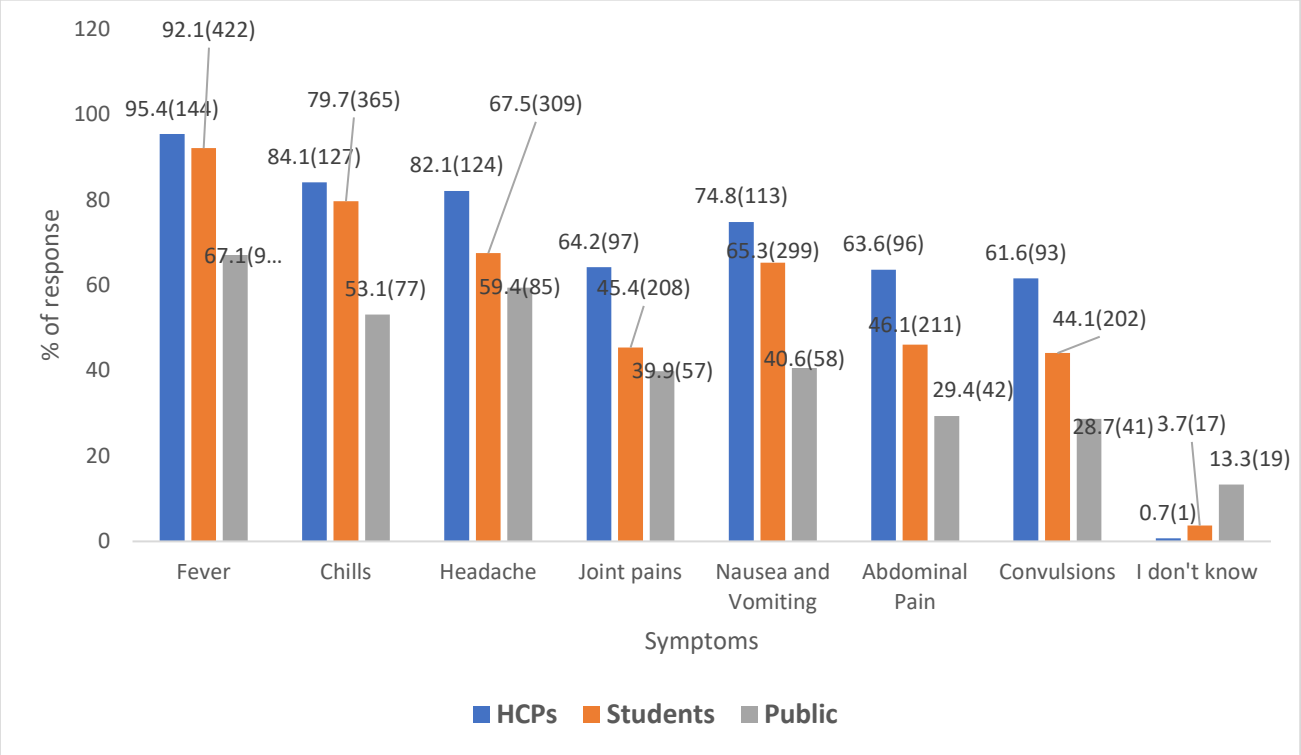


Figure 3.6: Distribution of knowledge of the South African respondents on malaria symptoms based on occupations.

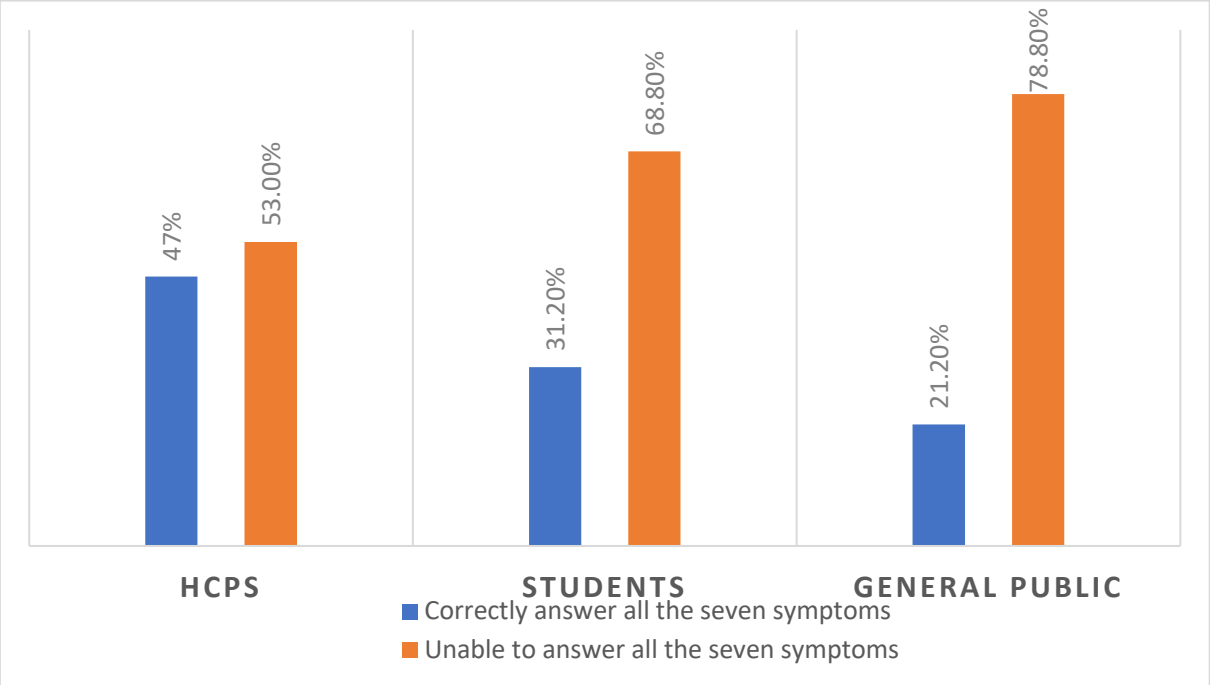


Figure 3.7: Distributions of percentage correct responses for all the symptoms across the different study groups.

The four most common symptoms and signs of malaria viz: fever, chills, headache and nausea and vomiting were identified by 46.2% (n = 529) of the participants. Within the groups, 59.4% (n = 187), 44.4% (n = 280) and 31.3% (n = 62) of the HCPs, students and public identified all the four common symptoms of malaria, respectively (p < 0.001).

3.2.2 Participant's knowledge on malaria vector

Out of the 1,144 participants, 91.8% (n = 1,034) mentioned infected female *Anopheles* mosquito as the responsible vector for malaria transmission, while 1.3% (n = 15) of the participants associated the cause of malaria to eating of contaminated food **(Figure 3.8).**

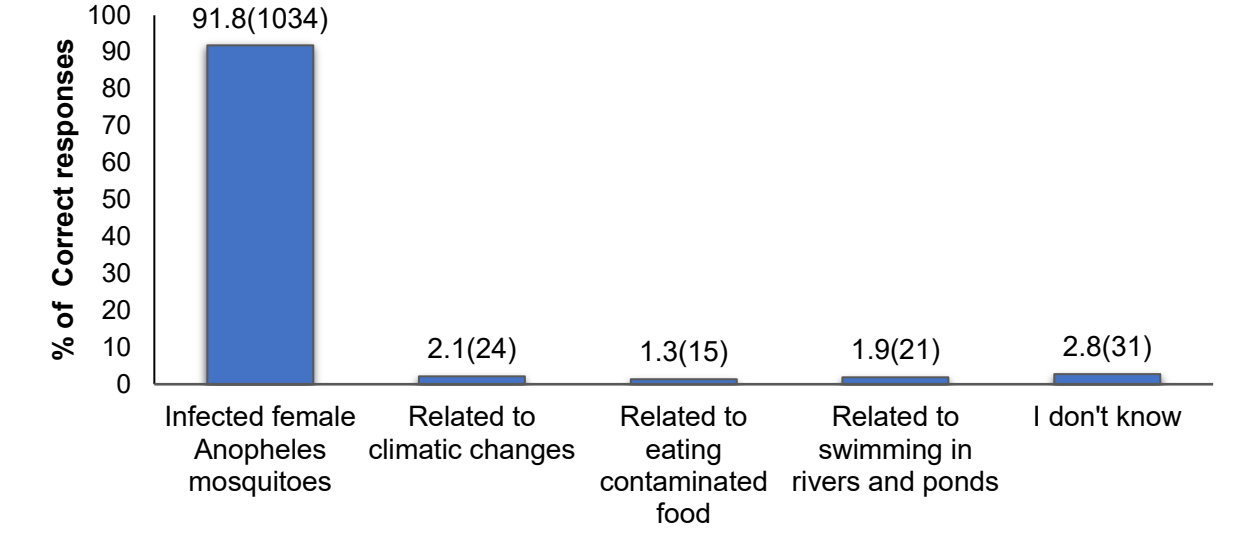


Figure 3.8: Distribution of participants responses on mode of transmission of malaria.

The study country of the respondents was found to have a statistically significant association with knowledge of malaria vector (p<0.001). Out of 15 participants that associated the cause of malaria with eating contaminated food 93.3% (n = 14) were from South Africa compared to 6.7% (n = 1) from Nigeria (Figure 3.9).

There was no statistically significant difference on knowledge of malaria vector among the students from the two study countries 96.5% (n = 166) from Nigeria compared to 96.2% (n = 436) from South Africa (p = 0.254). However, a slightly higher level of misconception was seen among the students from South Africa where 0.7% (n = 3) and 1.3% (n = 6) associated the cause of malaria with eating contaminated food and

swimming in the river and ponds, respectively, while none of the student from Nigeria have associated malaria with any of the above causative factor.

A statistically significant proportion of the HCPs 99.0% (n = 305) correctly associated female *Anopheles* mosquito as the vector responsible for malaria transmission compared to students and public (p<0.001) (Figure 3.10). Furthermore, a higher proportion of misconception on malaria vector was seen among the public 6.2% (n = 12) who associated the cause of malaria with eating contaminated food compared to students 0.7% (n = 3); while none of the HCPs associated the cause of malaria with eating contaminated food (Figure 3.10).

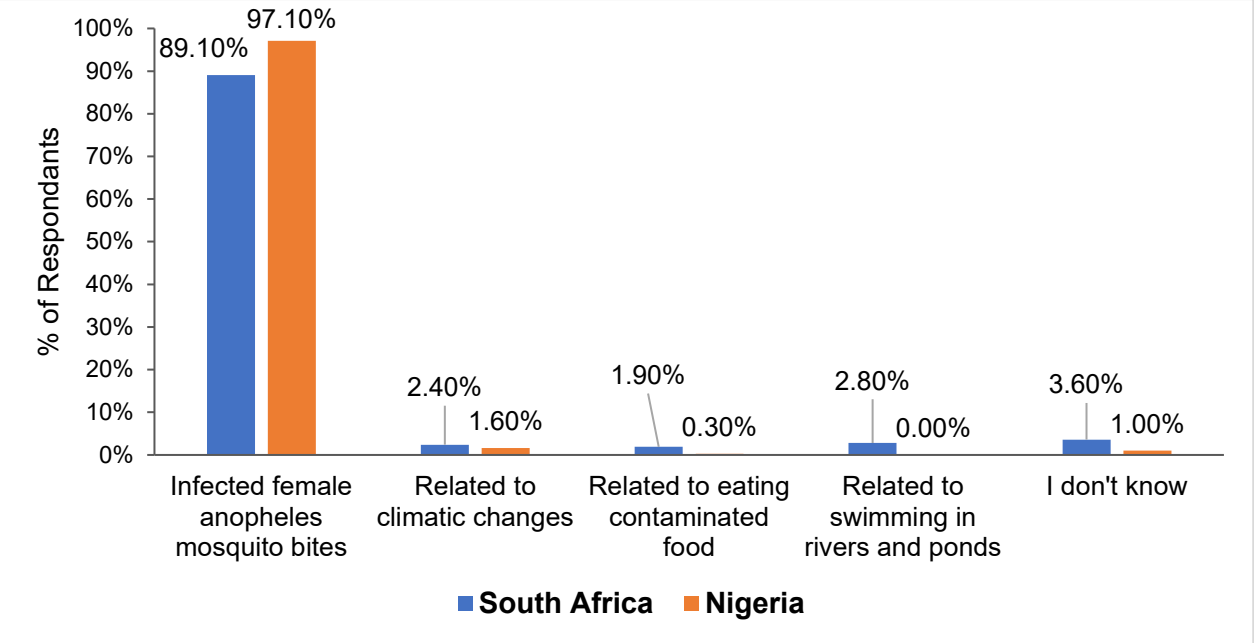


Figure 3.9: Distribution of participants knowledge on mode of malaria transmission across the study countries.

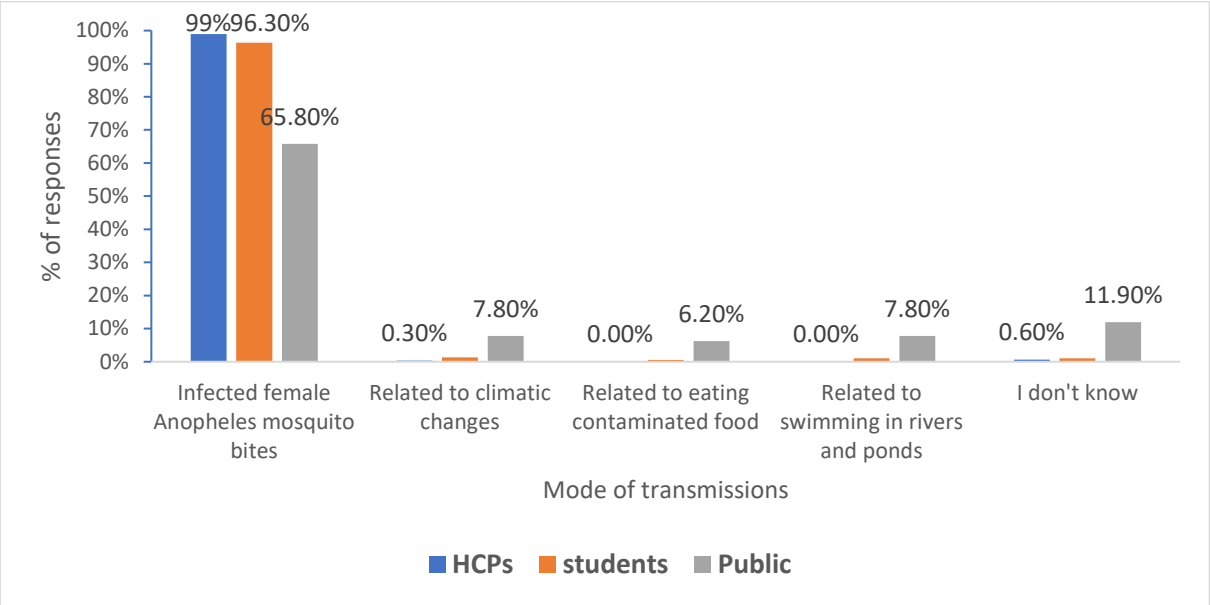


Figure 3.10: Distribution of the respondent's knowledge of malaria vector across the study groups.

Furthermore, the participants gender ($p=0.027$), level of educations ($p<0.001$) and occupational status ($p<0.001$) were found to be statistically significantly associated with knowledge of malaria vector. While the age of the participants was not statistically associated with knowledge of malaria transmission vector (Table 3.3).

Table 3.3: Knowledge of malaria vector across the respondents' demographics characteristics.

Charac-teristics % (n)	Female *Ano*pheles mosquito bite	Climatic changes	Contaminated food	Swimming in rivers and ponds	P values
Level of education					<0.001
No schooling	63.2(12)	0.0(0)	10.5(2)	5.3(1)	
Primary	50.0(4)	12.5(1)	0.0(0)	0.0(0)	
Secondary	86.7(208)	4.2(10)	2.5(6)	2.9(7)	
Tertiary	94.3(800)	1.5(13)	0.8(7)	1.5(13)	
Gender					0.027
Male	89.0(419)	3.0(14)	2.1(10)	1.9(9)	
Female	94.0(610)	1.4(9)	0.8(5)	1.8(12)	
Occupations					<0.001
HCPs	99.0(305)	0.3(1)	0.0(0)	0.0(0)	
Students	96.3(602)	1.3(8)	0.5(3)	1.0(6)	
Public	65.8(127)	7.8(15)	6.2(12)	7.8(15)	
Age					0.227
18-20yrs	91.4(223)	0.8(2)	1.6(4)	2.9(7)	
21-40yrs	92.0(676)	2.7(20)	1.5(11)	1.6(12)	
>40yrs	92.6(50)	1.9(1)	0.0(0)	0.0(0)	

3.2.1 Knowledge on mosquito breeding site and season of malaria transmission

Out of the total 1,144 participants, 85.3% (n = 962) correctly mentioned standing water as the breeding site for mosquito growth. While 7.2% (n = 81), all from South Africa reported not knowing the mosquito breeding site.

Furthermore, a higher proportion of participants from South Africa mentioned soil as the breeding site of mosquito 2.0% (n = 15) compared to those from Nigeria 1.3% (n = 5). However, there were more participants from Nigeria 8.9% (n = 34) that have a misconception on garbage as a mosquito breeding site compared to those from South Africa 4.2% (n = 31). There was a statistically significant association (p<0.001) between the knowledge of mosquito breeding site between the two study countries (Figure 3.11).

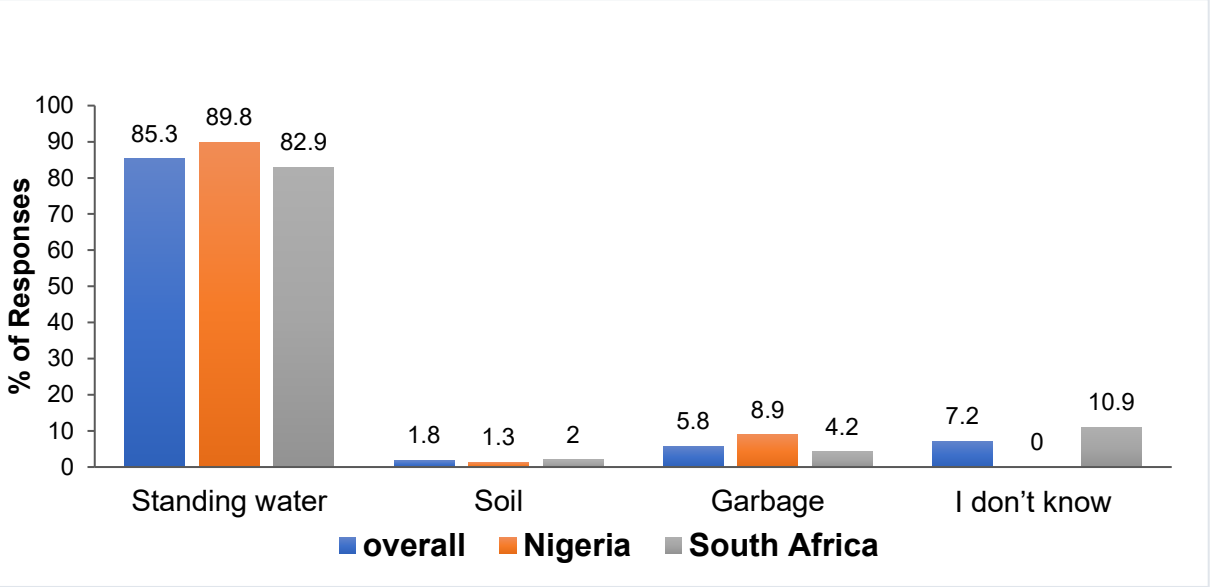


Figure 3.11: Respondent's overall knowledge on mosquito breeding sites (both countries combined) and within each country.

Among the different study groups, a higher proportion of HCPs (97.3%; n = 146) from South Africa correctly mentioned standing water as the mosquito breeding site, compared to (94.4%; n = 153) of their counterpart from Nigeria. However, a higher proportion of students (91.8%; n = 156) and public (69.2%; n = 36) from Nigeria correctly mentioned standing water as the breeding site for mosquito development compared to (87.3%; n = 397) and (53.2%;n = 740) of the students and public from South Africa, respectively (Figure 3.12).

A total of 79.5% (n = 893) correctly mentioned that the rainy season was the period with the highest malaria cases, while (6.7%; n = 75) of the respondents said there is no difference in the number of malaria cases between the different seasons in both countries (Figure 3.13). A statistically significant differences on the knowledge of malaria seasons was seen between the respondents from the study countries ($p<0.001$). A higher proportion of participants from South Africa (8.6%; n = 63) mentioned dry season as period with highest malaria transmission compared to (7.5%; n = 29) from Nigeria that mentioned dry season (Figure 3.14).

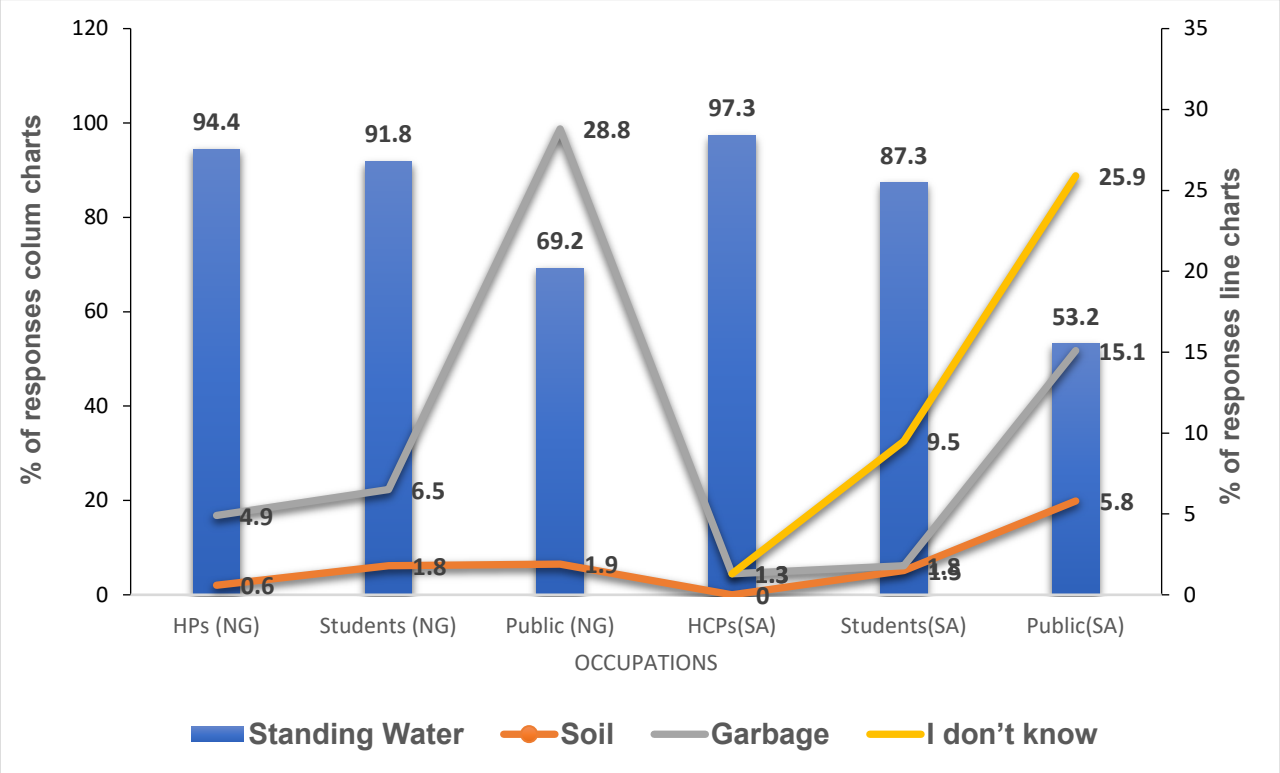


Figure 3.12: Combination chart depicting the percentage knowledge of mosquito breeding site among the different groups of respondents across the study countries.

Where: NG= Nigeria, SA= South Africa.

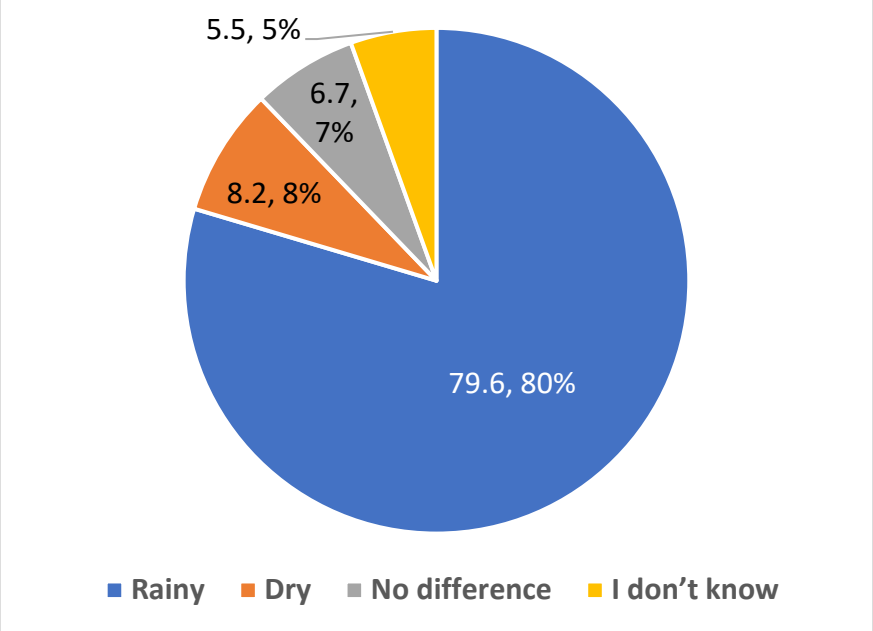


Figure 3.13: Pie chart depicting knowledge of malaria season of the study participants.

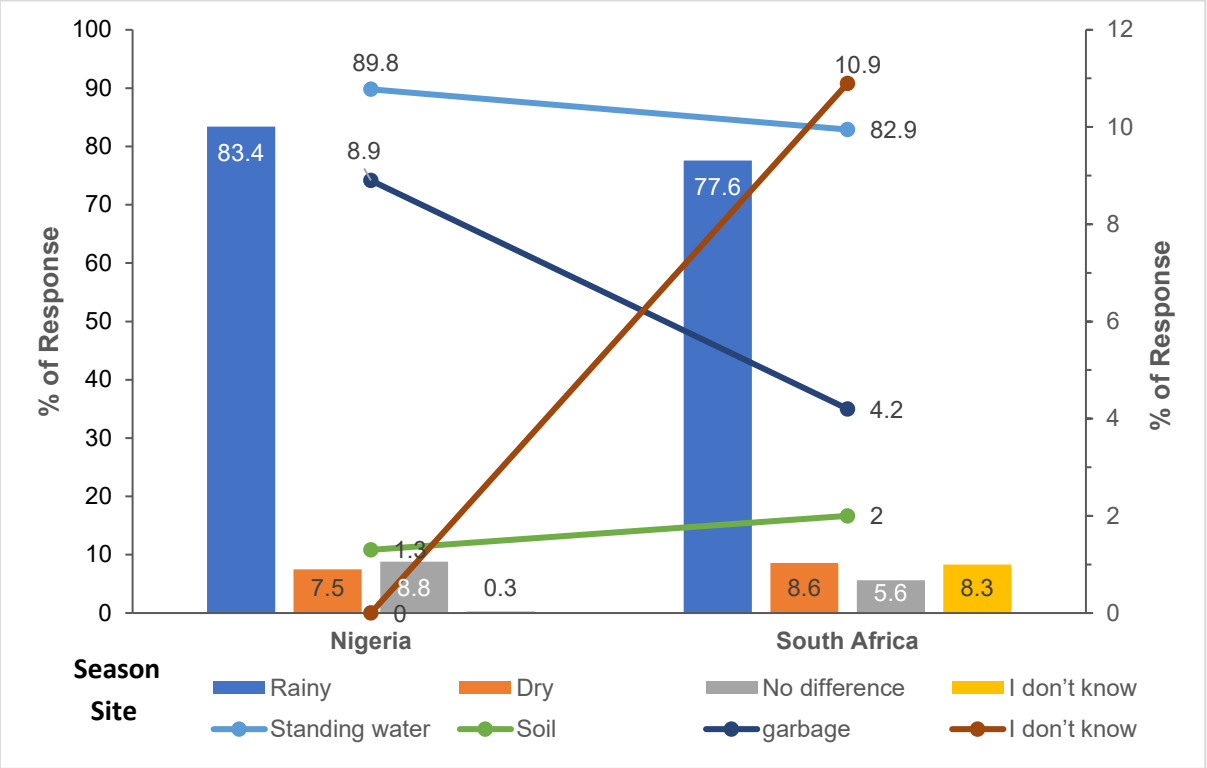


Figure 3.14: Cluster bar and line charts depicting the participants knowledge of malaria seasons and breeding sites across the two countries.

The existence of an association between the knowledge of mosquito breeding site and occupations was found to be statistically significant (p=<0.001) as determined using the Pearson chi-square. The participants level of education was found to be statistically related to the knowledge of mosquito breeding site (p<0.001) with those with tertiary level of education having the highest knowledge level (87.3%; n = 745) compared to (83.5%; n = 198), (50.0%; n = 4) and (26.3%; n = 5) for the secondary, primary and no schooling, respectively.

The knowledge of the mosquito breeding site was found to be highest among the respondents with age >40yrs (91.2%; n = 52) compared to (87.0%; n = 640) and (79.5%; n = 194) for those within the age range of 21-40yrs and 18 – 20yrs, respectively. However, this difference was not statistically significant (p = 0.068).

3.2.2 Knowledge on malaria control strategies

Participants were asked to select the strategies of malaria control they knew, six multiple choice options were presented to them which include: LLINs, IRS, malaria case management, health promotion, other strategies and I do not know options. Out of the 1,144 respondents, the majority (72.3%; n = 782) knew LLINs as a malaria control strategy, while (6.8%; n = 74) of the participants said they do not know any malaria control strategies (Table 3.4).

Table 3.4: Frequency and Percentage of the participants responses on malaria control strategies.

Characteristics	Frequency (n)	Percentage (%)
LLINs	782	72.3
IRS	478	44.2
Health promotion	472	43.7
Case management	267	24.7
Other control strategies	35	3.2
Don’t know any	74	6.8

A statistically significant differences were seen when comparing the knowledge of malaria control strategies across the three study populations, where the HCPs recorded a statistically higher knowledge on LLINs (83.5%; n = 237) compared to (74.1%; n = 453) and (49.5%; n = 92) from the students and public, respectively ($p<0.001$). While the students recorded a slightly higher knowledge on IRS (49.3%; n = 453) compared to (43.0%; n = 122) and (29.6; n = 92) from the HCPs and public, respectively ($p<0.001$) (Figure 3.15).

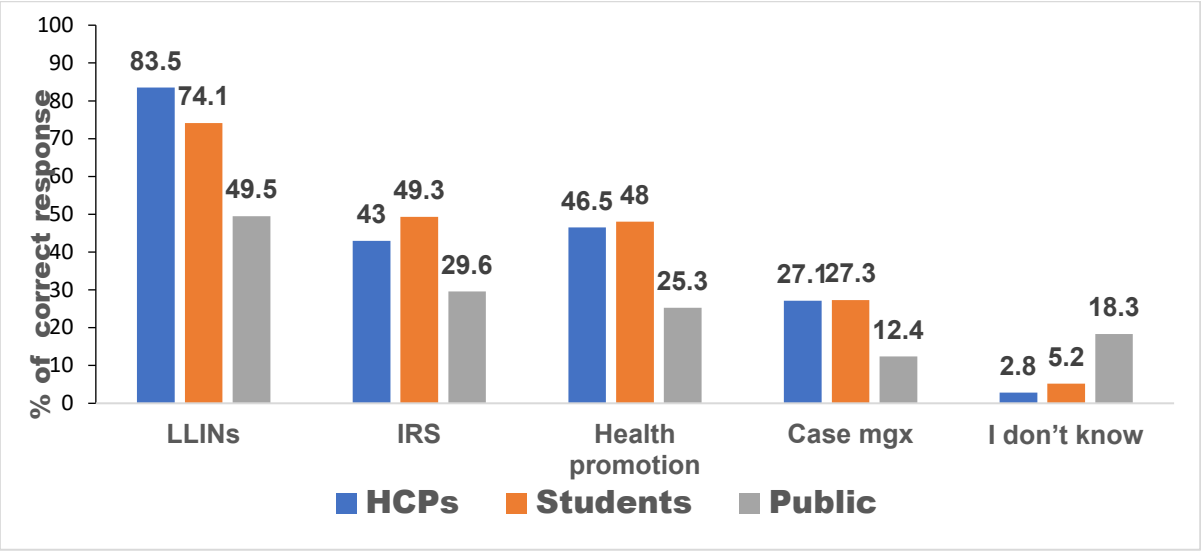


Figure 3.15: Distributions of knowledge of three different study groups on malaria control strategies.

The participants from South Africa have a statistically higher knowledge on the three of four control strategies assessed in this study (Table 3.5). However, a statistically higher proportion of respondents from Nigeria (84.5%; n = 295) mentioned LLINs as a malaria control strategy, compared to 66.5% (n = 487) from South Africa (p<0.001). Across the three study groups, the public respondents from Nigeria recorded the highest knowledge on LLINs (89.4%; n = 42) compared to HCPs (88.4%; n = 122) versus 78.8% (n = 115) and students 81.4% (n = 131) versus 72.0% (n = 322) from Nigeria versus South Africa, respectively.

Table 3.5: Distributions of respondents' knowledge on malaria control strategies across the two countries.

Characteristics	South Africa %(n)	Nigeria %(n)	X^2	P value
LLINs	66.5 (487)	84.5 (295)	13.120	<0.001
IRS	54.4 (398)	22.9 (80)	112.010	<0.001
Health promotion	53.4 (391)	23.2 (81)	104.371	<0.001
Case management	30.9 (22)	11.7 (41)	55.292	<0.001
Don't know	9.2 (67)	2 (7)	21.615	<0.001

A significantly higher proportion of HCPs (61.6%; n = 90) from South Africa recorded higher knowledge on IRS compared to (23.2%; n = 32) from their counterpart in Nigeria (p<0.001) (Table 3.6).

Table 3.6: Distributions of respondents' knowledge on malaria control strategies of the different study groups across the two countries.

Variable	South Africa %(n)			Nigeria %(n)			χ^2
	HCPs	Students	Public	HCPs	Students	Public	
LLINs	78.8(115)	72.0(322)	37.0(50)	88.4(122)	81.4(131)	89.4(42)	54.207*
IRS	61.6(90)	59.1(264)	32.6(44)	23.2(32)	23.0(37)	13.8(11)	26.261*
Health promotion	66.4(97)	57.7(258)	26.7(36)	25.4(35)	21.7(35)	23.4(11)	32.109*
Case Mgx	36.3(53)	34.7(155)	8.0(18)	17.4(24)	7.5(12)	10.6(5)	18.871*
Don't know	4.8(7)	6.0(27)	24.4(33)	0.7(1)	3.1(5)	2.1(1)	47.564*

3.2.3 Respondents' knowledge on malaria as a cause of anaemia and family history of blood transfusion due to malaria

Participants were asked if a malaria infection can cause anaemia and if they or any member of their families had ever been given a blood transfusion due to malaria-induced anaemia. Out of the 1,144 participants, (79.8%; n = 893) responded that malaria could cause anaemia; whilst (20.2%; n = 226) responded "no". A significantly higher proportions of Nigerians (84.3%; n = 322) were aware about the anaemia from a malaria infection, compared to (77.5%; n = 571) from South Africa (OR=0.641, 95%CI=0.463-0.887, p=0.007). A significantly higher proportion of HCPs (93.2%; n = 289) said 'malaria can cause anaemia' compared to students and public participants (p=0.001).

Of the 1,144 participants, a positive family history of blood transfusion due to anaemia from malaria infection was obtained from only (14.6%; n = 163). The positive history of blood transfusion was statistically significantly reported by the participants from Nigeria

(33.7%; n = 126) compared to (5.0%; n = 37) from South Africa ($p < 0.001$). A higher proportions of positive family history of blood transfusion was obtained from all the study groups in Nigeria (44.4%; n = 24), (41.8%; n = 64) and (22.8%; n = 38) compared to (11.6%; n = 16), (8.1%; n = 12) and (2.0%; n = 9) for the public, HCPs and students from Nigeria and South Africa respectively. (Figure 3.16).

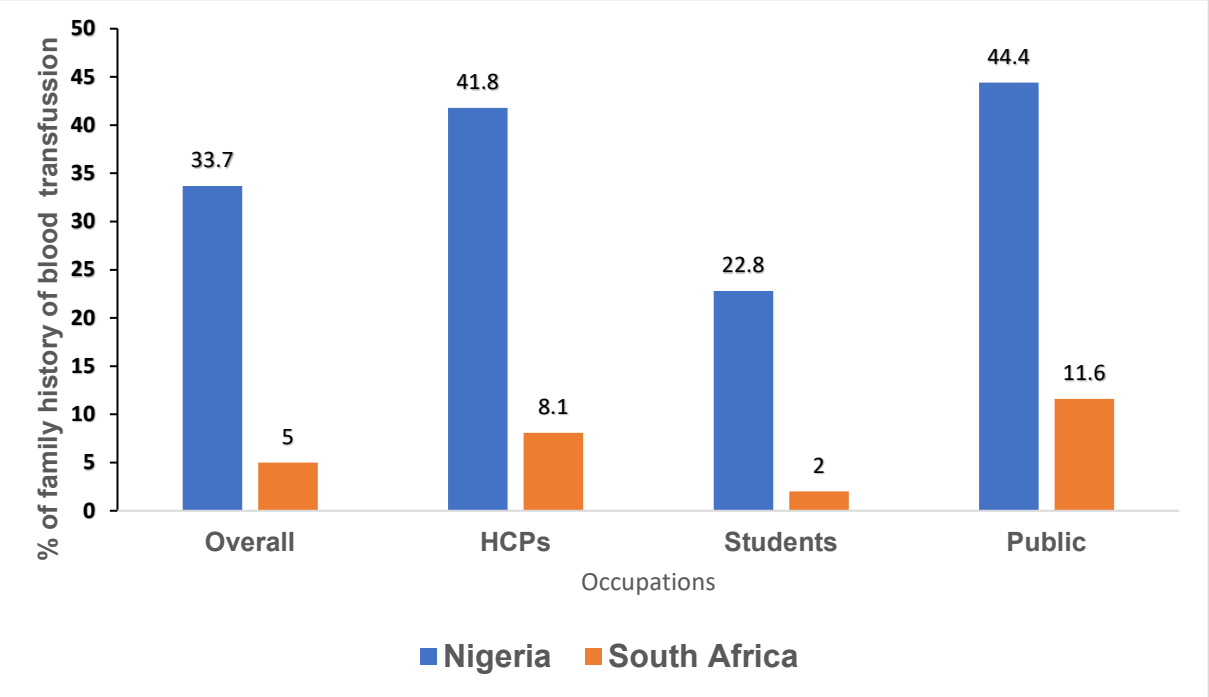


Figure 3.16: The participant responses on the family history of blood transfusion due to anaemia from three different research groups across the study countries.

3.2.4 Sources of malaria information and participants request for further health promotion on malaria

The participants were asked to identify their source of malaria-related information. A range of options were provided which include radio and television, hospitals, schools, friends, newspapers, and other sources. The participants were also asked if they think they have enough information on malaria and if not what kind of health promotion will be of interest to them.

Overall, majority of the participants mentioned schools as their main source of information on malaria 55.5% (n = 609). While the least source of information was newspapers 6.7% (n = 72) (Figure 3.17). For the participants from Nigeria the highest source of information on malaria was hospitals 46.8% (n = 168), while for the South African respondents the highest source of information on malaria was from schools.

The participants from South Africa have an odd twice more likely to obtain an information on malaria from schools compared to those from Nigeria (OR = 2.114; 95% CI= 1.649–2.711; p<0.001), the South Africans participants were also twice as likely to obtain an information on malaria from friends and newspapers compared to Nigerians (Table 3.7).

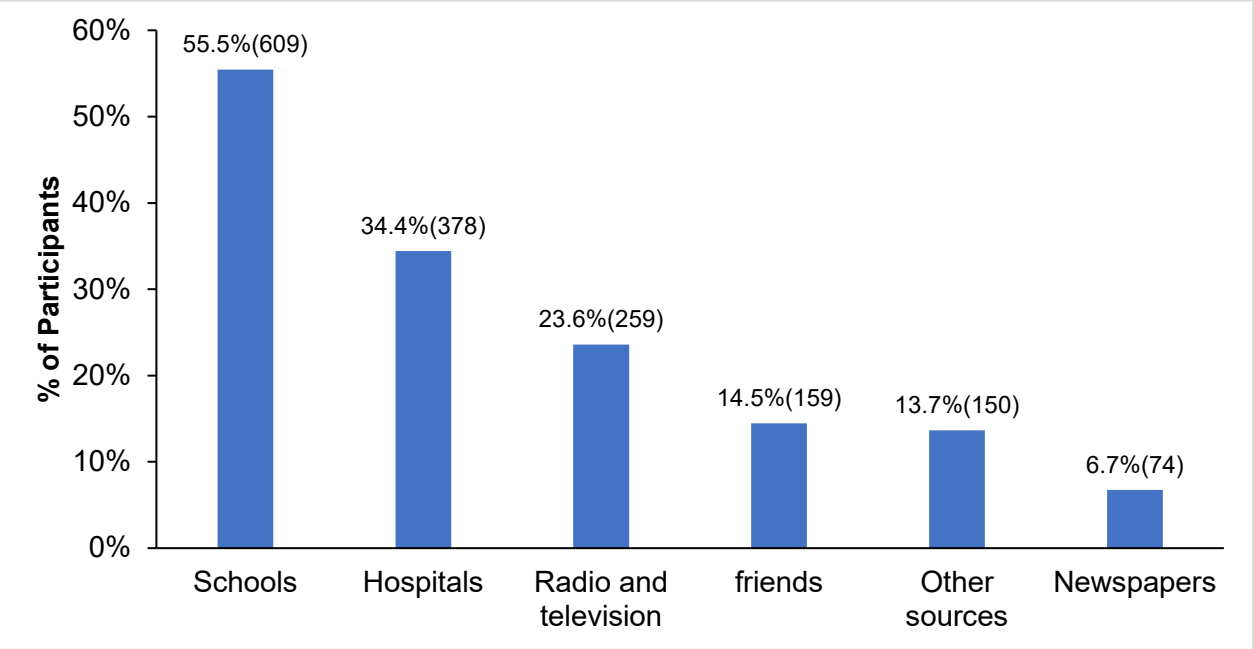


Figure 3.17: Overall distribution of participants source of information on malaria.

In contrast, a higher proportion of participants from Nigeria (34.0%; n =122) received their information from radio and television compared to (18.5%; n = 137) from South Africa. Also, more participants from Nigeria (46.8%; n = 168) received their information on malaria from the hospitals compared to (28.4%; n = 210) of the participants from South Africa. The participants from South Africa have an odd 0.493 and 0.517 less likely to obtain an information on malaria from radio / television and from the hospitals respectively compared to participants from Nigeria (Table 3.7). Apart from the above sources of malaria information, other information sources on malaria were mentioned by 13.7% (n = 150) of the study participants; the guidelines, books, journals, and conferences were the highest additional sources of malaria information mentioned by 2.4% (n = 27) of the respondents (Table 3.8).

Table 3.7: Respondent's malaria source of information and adjusted odds ratios across the two study countries.

Variables	South Africa %(n)	Nigeria %(n)	OR (95% CI)	P values
Radio, Television	18.5(137)	34.0(122)	0.493(0.372-0.654)	<0.001
Hospitals	28.4(210)	46.8(168)	0.517(0.400-0.667)	<0.001
Schools	60.6(448)	44.8(161)	2.116(1.649-2.711)	<0.001
Friends	17.5(129)	8.4(30)	2.499(1.645-3.795)	<0.001
News papers	7.8(58)	4.5(16)	1.964(1.113-3.464)	0.018

Table 3.8: Other sources of malaria information reported by the participants.

Characteristics	Frequency (n)	Percentage (%)
Guidelines, books, journals, conferences	27	2.4
Internet	20	3.1
Family	18	1.6
Pamphlets	2	0.2
Movies	2	0.2
WITS Museum	1	0.1
Personal studies	3	0.3
Workplace	1	0.2

Among the 1,144 participants, (48.1%; n = 544) said they have enough information on malaria, while (51.9%; n = 586) said they do not have enough malaria information and they requested for further health promotion on malaria. Most of the requested information were those related to malaria treatment (58.6%; n = 337) and those related to the preventive measures (54.6%; n = 314). A higher proportion of South Africans requested virtually all the forms of information on malaria compared to Nigerians except for the information on control measures which was requested by a slightly higher proportions of the participants from Nigeria (48.2%; n = 41) compared to (47.3%; n = 232) of the respondents from South Africa (Table 3.9).

3.2.5 Overall malaria-related Knowledge Score of the respondents

The overall malaria knowledge was computed by summing the individual scores of the participants on malaria knowledge related questions (Table 2.2). Out of the 1,144 participants (68.8%; n = 779) have good knowledge on malaria, with a score ≥8/16, while (31.2%; n = 355) have poor knowledge, with a score of ≤ 7/16. A significantly higher proportion of respondent from South Africa have good knowledge of malaria (73.8%; n = 548) compared to the respondents from Nigeria (59.2%; n = 231) (p <0.001), with an odd almost two times more likely for South African respondents to have good malaria-related knowledge compared to those from Nigeria (OR=1.934, 95% CI=1.492-2.504).

Table 3.9: Different types of information on malaria requested by the participants.

Information requested	Overall %(n)	South Africa %(n)	Nigeria %(n)	OR (95%CI)	P values
Information on treatment.	58.6(337)	70.8(291)	63.9(146)	4.748 (3.377-6.676)	<0.001
Information on prevention.	54.6(314)	66.4(273)	56.9(41)	4.879 (3.418-6.966)	<0.001
Information on control.	47.5(273)	56.4(232)	56.9(41)	3.820 (2.669-5.467)	<0.001
Nature of the disease.	43.7(251)	44.1(213)	7.9 (38)	3.681 (2.542-5.331)	<0.001
Signs and symptoms.	45.4(261)	57.9(238)	31.9(23)	7.429 (4.744-11.632)	<0.001
Other Information.	1.2(7)	1.7(7)	2.8(2)S	1.832 (0.379-8.862)	0.445

Good malaria knowledge was found to be significantly associated with level of education, with highest good knowledge on malaria (71.1%; n = 608) seen among those with tertiary level of educations (p <0.034). Malaria-related knowledge was also

found to be associated with gender, with a higher proportion of females having good knowledge (72.1%; n = 470) compared to males (64.3%; n = 305) (p= 0.022).

A statistically significant association was also seen between good knowledge on malaria and age of the respondents with those within the age range of 21 to 40yrs having the highest knowledge (72.5%; n = 537) compared to (69.6%; n = 39) and (59.0%; n = 144) for > 40yrs and 18 to 20yrs respectively (p<0.001). The participant within the age of 40yrs and above from South Africa has a significantly higher knowledge of malaria (82.1%; n = 23) compared to those from Nigeria (57.1%; n = 16) (p= 0.042).

A significantly higher proportions of HCPs have good knowledge of malaria (77.5%; n = 244) compared with (71.3%; n = 448) and (45.5%; n = 87) among the students and public respondents respectively p<0.001. A significantly higher proportions of HCPs (88.1%; n = 133) and Students (79.3%; n = 361) from South Africa have good malaria-related knowledge compared to (68.1%; n = 111) and (50.3%; n = 87) for HCPs and students from Nigeria respectively (Table 3.10). However, a significantly higher knowledge level (61.1%; n = 33) was seen among the public respondents from Nigeria compared to (39.4%; n = 54) in South Africa (p=0.007).

Table 3.10: Malaria-related knowledge distribution across the respondent's socio-demographic characteristics.

Characteristics	Total % (n)		South Africa % (n)		Nigeria% (n)		P value
	Good	Poor	Good	Poor	Good	Poor	
Overall knowledge score	68.8(779)	31.2(354)	73.8(548)	26.2(195)	59.2(231)	40.8(159)	<0.001
Gender							0.022
Females	72.1(470)	27.9(183)	76.5(355)	23.5(110)	61.2(115)	38.8(73)	
Males	64.3(305)	35.7(169)	69.5(189)	30.5(83)	57.4(116)	42.6(86)	
Occupations							<0.001
HCPs	77.7(244)	22.2(70)	88.1(133)	11.9(18)	68.1(111)	31.9(52)	<0.001
Students	71.3(448)	28.7(181)	79.3(361)	20.9(120)	50.3(87)	49.7(86)	<0.001
Public	45.5(87)	52.5(104)	39.4(54)	60.6(83)	61.1(33)	38.9(21)	0.007
Education							0.034
No schooling	57.9(11)	42.1(8)	28.6(2)	71.4(5)	75.0(9)	25.0(3)	0.048

Primary	57.1(4)	42.9(3)	40.0(2)	60.0(3)	100(2)	-	0.147
Secondary	62.1(149)	37.9(91)	68.3(140)	31.7(65)	25.7(9)	74.3(26)	<0.001
Tertiary	71.1(608)	28.9(247)	76.6(401)	23.2(121)	62.2(207)	37.8(126)	<0.001
Age category							0.004
18-20yrs	59.0(144)	41.0(100)	63.1(111)	36.9(65)	48.5(33)	51.5(35)	
21-40yrs	72.5(537)	27.5(204)	76.9(380)	23.1(114)	63.6(157)	36.4(90)	
>40yrs	69.6(39)	30.4(17)	82.1(23)	17.9(5)	57.1(16)	42.9(12)	

3.3 Attitudes and Practices on Malaria

This section presents the result obtained from the analysis of participants attitude on malaria management and preventive practices.

3.3.1 Attitudes on malaria infections and treatment seeking behaviours

Participants were asked if malaria can be prevented and how soon will they seek treatment after suspecting they have malaria-related signs and symptoms. Out of the 1,144 participants, (93.6%; n = 1,013) said yes malaria can be prevented with an early treatment, while (6.4%; n = 69) understood that malaria is not a preventable disease, with (6.3%; n = 45) and (6.6%; n = 24) in South African and Nigeria, respectively. There are almost equal proportions of the participants that believed malaria can be prevented from both countries (93.7%; n = 672) from South Africa versus (93.4%; n = 341) from Nigeria (p=0.849).

Within the different study groups, (96.9%; n = 279), (95.7%; n = 581) and (81.8%; n = 151) of the HCPs, students and public indicated that malaria is a preventable disease (p<0.001). The HCPs (97.9%; n = 139) and public (83.2%; n = 114) from South Africa shows a slightly higher proportion of knowledge on malaria as a preventable disease ompared to Nigerian HCPs (95.9%; n = 140) and public (78.0%; n = 39). However, a slightly higher proportion of the students (95.9%; n = 162) from Nigeria mentioned malaria is a preventable disease compared to (95.7%; n = 419) from South Africa.

Most of the participants (56.5%; n = 596) said they will seek an early treatment within 24 hours of suspecting they were infected with malaria, while (4.7%; n = 50) said they will wait till after seven days or more (Figure 3.18). There is a statistically significant differences on treatment seeking behaviours between the study participants from the two study countries (p<0.001). A higher proportion of respondents from South Africa

(59.6%; n = 406) said they will seek treatment within 24 hours compared to (50.8%; n = 190) from Nigeria. Furthermore, a higher proportion of participants from Nigeria (6.4%; n = 24) said they will wait for 7 days and longer before seeking treatment compared to (3.8%; n = 12) from South Africa.

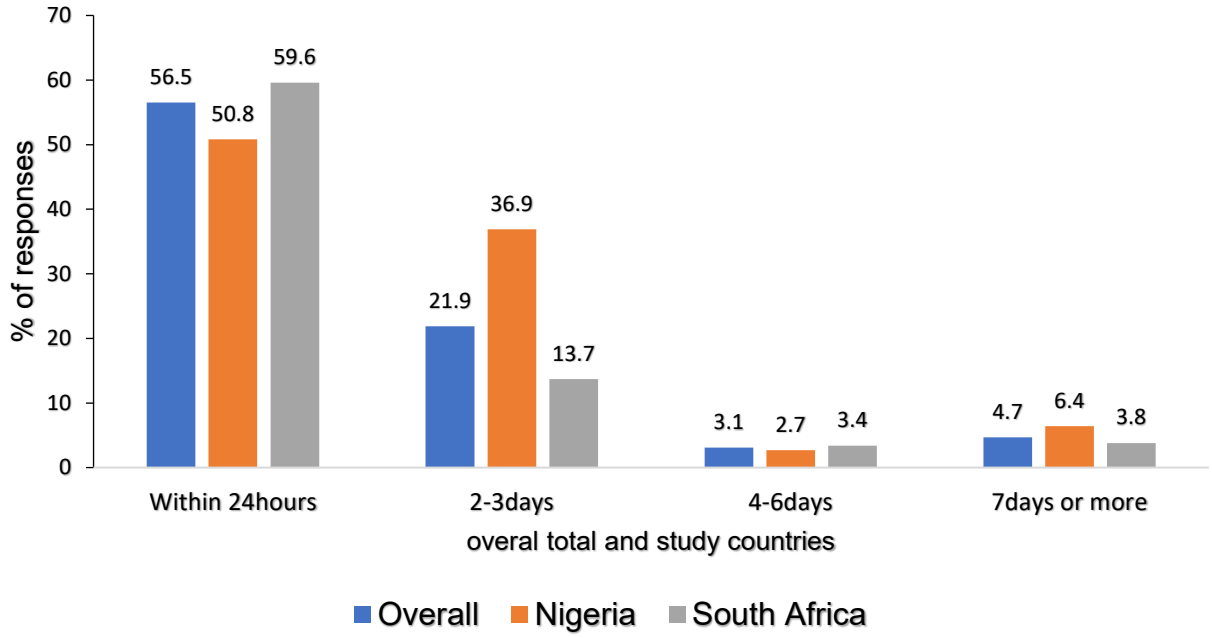


Figure 3.18: Clustered bar chart depicting the distribution of the participants malaria treatment seeking behaviours overall and across the study countries.

The majority of those that would seek an early treatment within 24 hours were HCPs (63.0%; n = 182), while the majority that said they will wait till 7days, or more were public respondents (10.8%; n = 20). When asked why they will not seek an early treatment, (5.8%; n = 66) of the study participants said they would use over the counter medications, while the most dangerous statement was from (0.7%; n = 8) of the study participants that said they will wait until the symptoms get worse (Figure 3.19). A statistically significant differences exist on the reasons for not seeking an early treatment between the two countries (p=0.001).

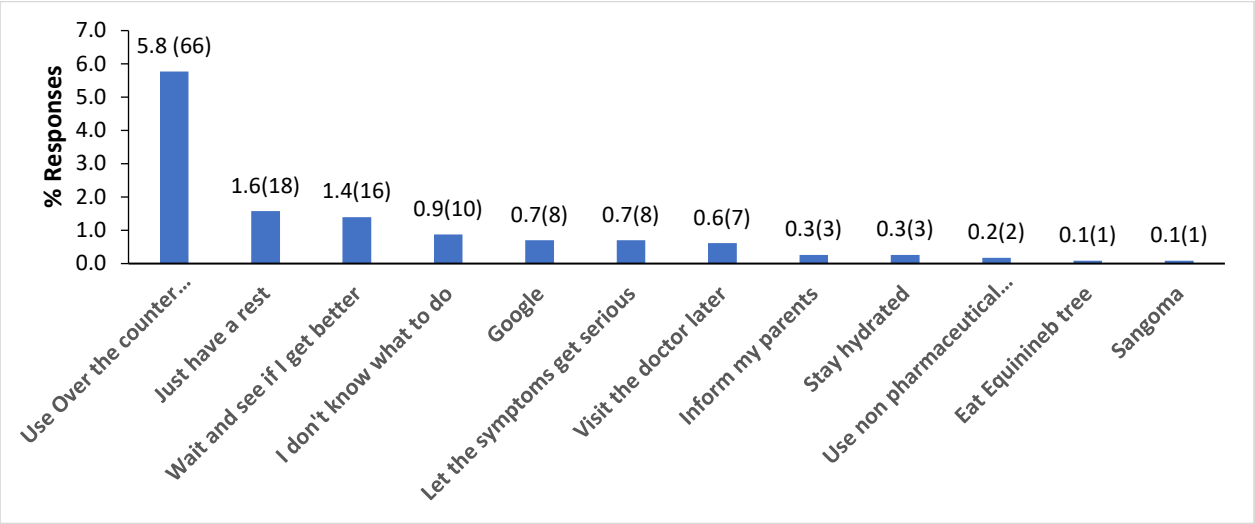


Figure 3.19: Simple bar charts showing the reasons provided by the respondents for not seeking an early treatment.

There were a higher proportion of participants from Nigeria (8.2%; n = 32) that said they will use over the counter medication compared to (4.5%; n = 34) from South Africa, while the participants that said they will wait until the symptoms get serious were all from South Africa. Interestingly out of the eight participants that said they will wait until the symptoms becomes serious (87.5%; n = 7) were students, while (12.5%; n = 1) was HCPs.

The treatment seeking behaviour was found to be statistically significant across the participants level of education (p=0.002), with majority of those with tertiary level of education willing to go for an early treatment (57.4%; n = 460) compared to (26.3%; n = 5) of Non schooling participants. Furthermore, a higher proportion of those with only primary level of education (28.6%; n = 2) and non-schooling (21.1%; n = 4) said they will wait for 7days or more before they will seek treatment.

The treatment seeking behaviour was also significantly difference across gender (p<0.001) with more females (59.4; n = 353) preparing an early treatment compared to males (53.5%; n = 243).

In South Africa a statistically significant differences exist between the treatment seeking behaviours and gender (0.001) where a significantly higher proportions of females (65.1%; n = 269) prepared an early treatment compared to males (52.5%; n = 137). In contrast in Nigeria there was no significant differences between the participants gender and treatment seeking behaviours (p = 0.093), but a slightly higher proportion of males (54.9%; n = 106) prepared an early treatment compared to females (46.4%; n = 84).

The treatment seeking behaviours was also statistically significantly difference across the participants age groups (p=0.011), the participants within the age of ≥ 40 years prepared an early treatment compared to those below 40 years of age.

3.3.2 Personal protective measures and previous history of malaria infections

Perticipants were provided with an options on personal protective measures which include: long lasting insecticide treated treated nets, mosquito repellents, clean environment and anti- malarial prophylaxis, they were asked to identify the personal protective measures they knew and also provided with an opportunity to mention more. Out of the 1,144 participants (81.3%; n = 817) mentioned LLINs as the most reliable personal protective measure, followed by mosquito repellents mentioned by (73.7%; n = 741), while the least mentioned personal protetive measure was clean environment (64.5%;n = 648) (Table 3.11).

More respondents from South Africa mentioned mosquito repellent (82.7%; n = 555) compared to (55.7%; n = 186) from Nigeria, and there is odds three times more likely for South African participants to used mosquito repellent for personal protection compared to participants from Nigeria (OR = 3.120, 95% CI = 2.415-4.032, p < 0.001); there is also an odd of almost four times more likely for South African to used antimalarial prophylaxis for malaria protection compared to participants from Nigeria (OR = 3.722, 95% CI = 2.880-4.809, P<0.001).

Table 3.11: Distributions of participants perceived personal protective measures across the study countries.

Characteristics	LLINs	Mosquito repellents	Clean environment	Anti-malarial prophylaxis
Overal %(n)	81.3 (817)	73.7 (741)	64.5 (648)	67.7 (680)
Nigeria %(n)	82.9 (277)	55.7 (186)	63.8 (213)	45.5 (152)
South Africa %(n)	80.5 (540)	82.7 (555)	64.8 (435)	78.7 (528)
OR (95% CI)	1.057 (0.808-1.384)	3.120 (2.415-4.032)	1.153 (0.902-1.475)	3.722 (2.880-4.809)
P values	0.684	<0.001	0.256	<0.001

However there were more respondents from Nigeria that mentioned LLINs (82.9%; n = 277) compared to (80.5%; n = 540) but the difference was not significant statistically (p = 0.684) (Table 3.11).

Overall, only 36.5% (n = 387) of the total respondent had personal experience of malaria infection/s in the past, where the majority were from Nigeria (89.9%; n = 348) versus 10.1% (n = 39) from South Africa. Furthermore, almost all the respondents from Nigeria (96.5%; n = 348) had a personal experience of a malaria infection compared to 5.6% (n = 39) from South Africa (p < 0.001) (Figure 3.20).

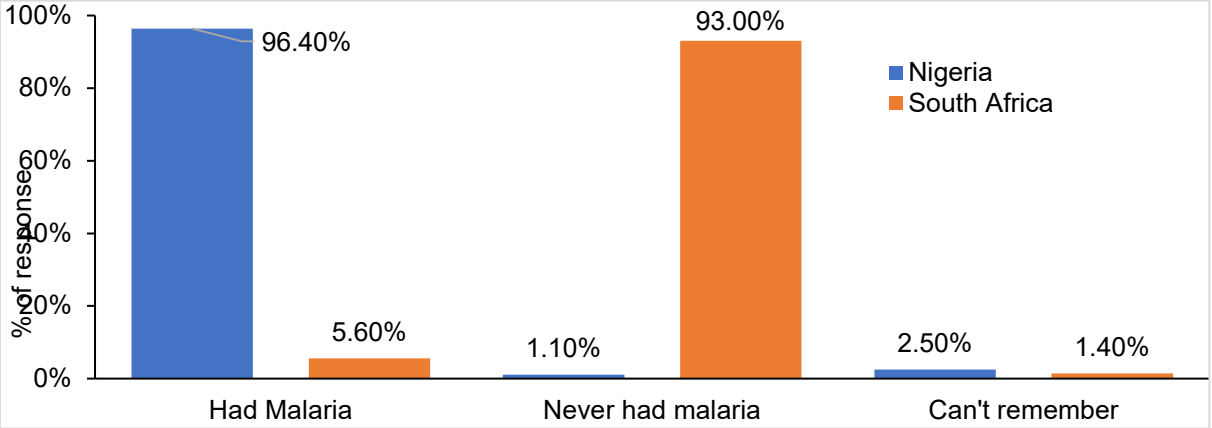


Figure 3.20: Distribution of participants that experienced malaria infection across the study countries.

3.3.3 Overall attitude Score

The participants' attitude and practices on malaria was computed by totalling their scores on the questions that assessed their attitudes towards malaria and their practices for malaria prevention (Table 2.3). The total score obtainable ranged from 0 to 10, any participants with a score greater than or equal to 50% (≥ 5/10) of the total scores obtainable is regarded as having a good attitude, while those with a score less than 50% (0 to 4/5) of the total scores obtainable is regarded as having a poor attitude.

Out of the 1,144 respondents, (56.6%; n = 648) demonstrated a good attitude on malaria with a statistically higher proportion of participants from South Africa (61.8%; n = 465) that have good atittude on malaria compared to (46.7%; n = 183) from Nigeria (p < 0.001) (Figure 3.21). The attitude score was associated with participants gender, educational status, occupational status and age (Table 3.12).

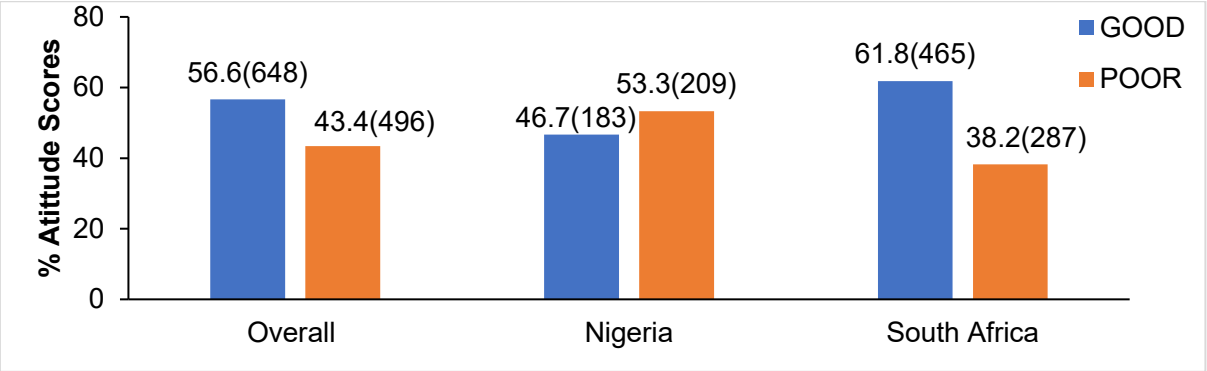


Figure 3.21: Clustered bar charts depicting the attitude scores of respondents (Total and across the study countries).

Table 3.12: Cross tabulation of respondent attitude score across socio-demographics.

Characteristics	Good	Poor	P value
Gender			0.014
Male	51.8(249)	48.2(232)	
Female	60.4(396)	39.6(260)	
Educational status			<0.001
No schooling	15.0(3)	85.0(17)	
Primary	25.0(2)	75.0(6)	
Secondary	50.0(121)	50.0(121)	
Tertiary	60.2(518)	39.8(343)	
Occupational status			<0.001
HCPs	62.9(198)	37.1(117)	
Students	61.8(390)	38.2(241)	
Public	30.3(60)	69.7(138)	
Age			0.002
18-20yrs	48.8(120)	51.2(126)	
21-40yrs	60.9(454)	39.1(292)	
>40yrs	49.1(28)	50.9(29)	

The HCPs from South Africa (76.2%; n = 115) demonstrated a statistically higher level of good attitude on malaria compared to (50.6%; n = 83) of HCPs from Nigeria (OR = 3.117. 95%CI = 1.922-5.056, P < 0.001). Furthermore, a statistically higher proportion of students from South Africa (67.9%; n = 311) have good atittude on malaria compared to (45.7%; n = 83) from Nigeria (OR = 2.517, 95%CI = 1,760-5.056, P < 0.001). However, there is higher proportion of public respondents from Nigeria (38.2%; n = 21) with good attitude score compared to (27.3%; n = 39) from South Africa but the difference was not significant statistically (OR = 0.607, 95%CI(0.315-1.171, p = 0.135) (Figure 3.22 and 3.23).

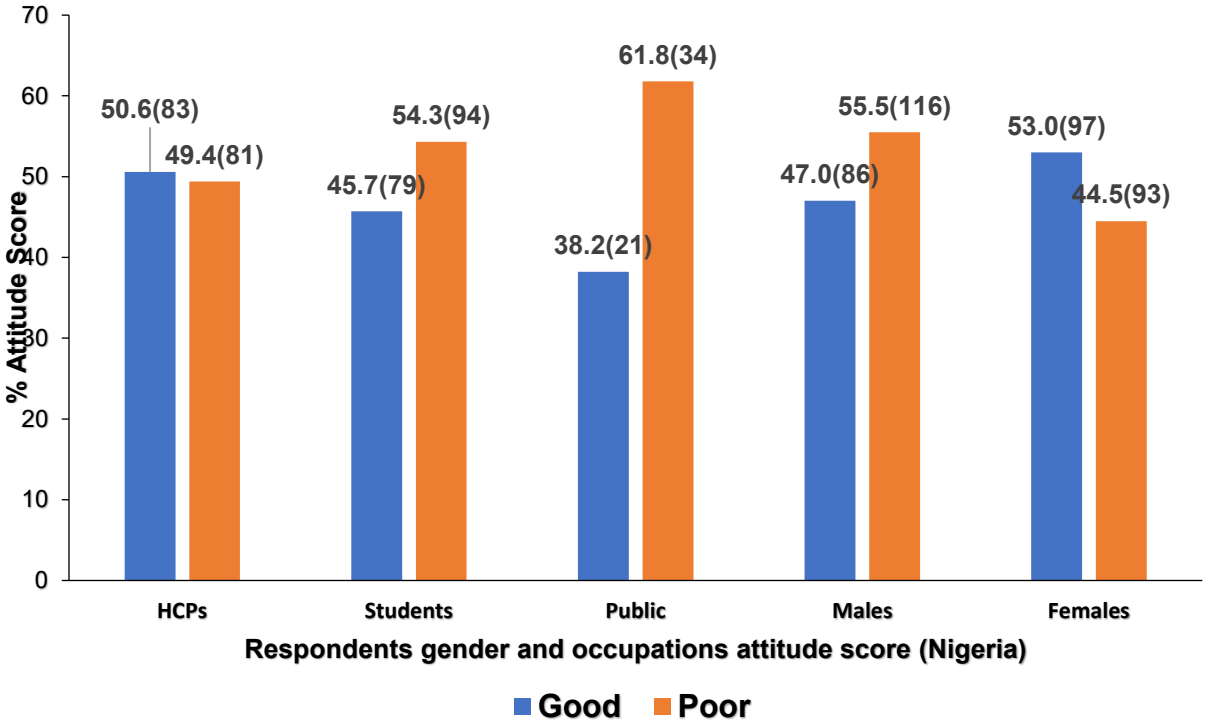


Figure 3.22: Attitude scores from different occupations and gender of Nigerian respondents.

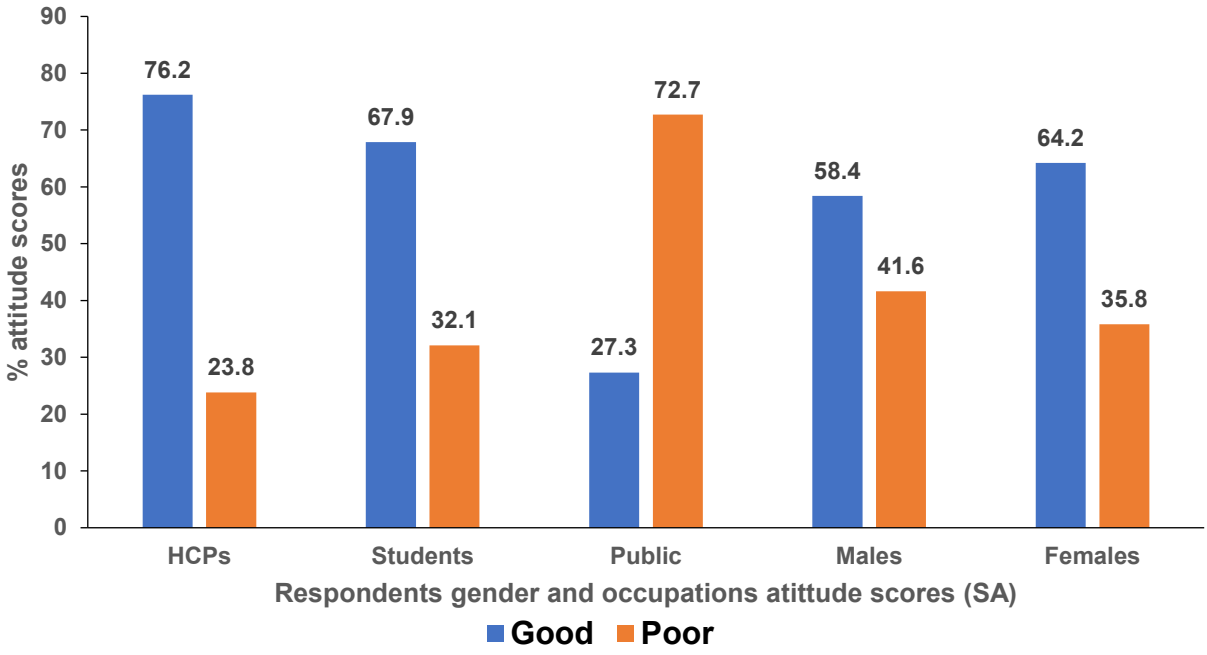


Figure 3.23: Attitude scores from different occupations and gender of South African respondents.

3.3.4 Mosquito repellents usage, commonly used products and reported side effects

The participants were asked if they have ever used mosquito repellents and if yes, can they remenber the products they have used and if they have ever experienced any side effects associated with repellents used.

In general there was a total of (82.1%; n = 883) of the study participants that used mosquito repellents in the past and there were slightly more participants in Nigeria (84.5%; n = 305) that used mosquito repellents compared to (80.8%; n = 578) from South Africa, but the difference was not statitistically significant (p = 0.141) (Figure 3.24).

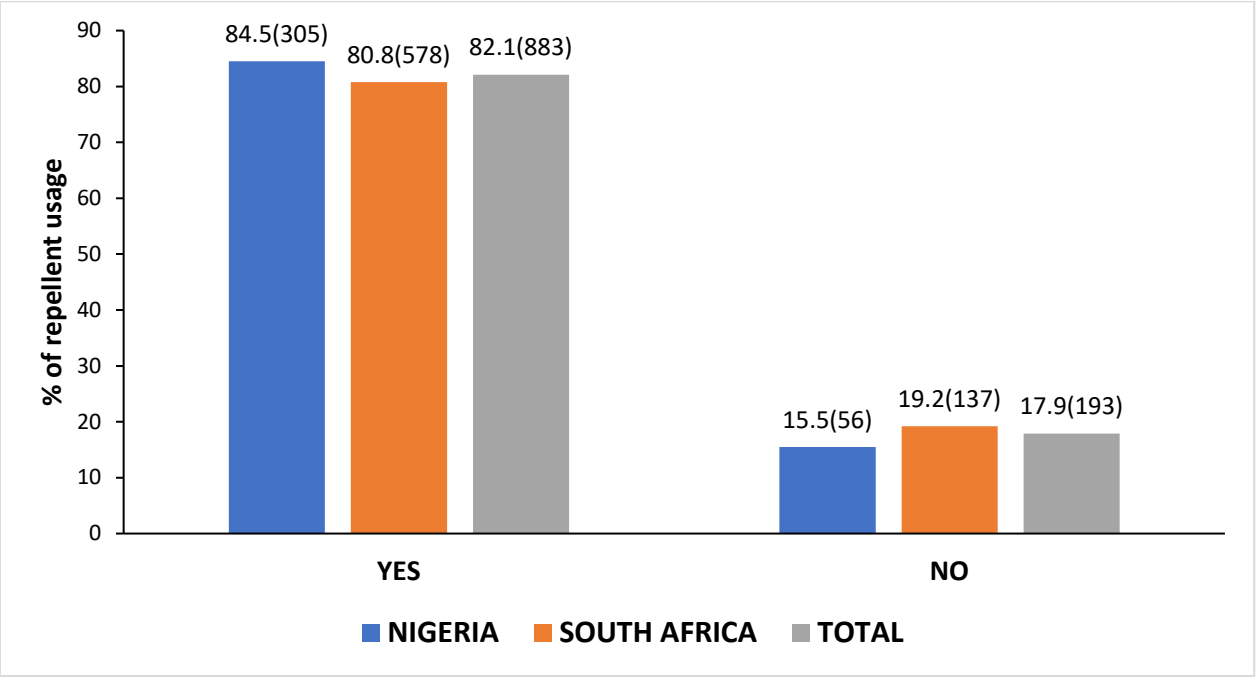


Figure 3.24: Distributions of Repellent use among the study participants from Nigeria and South Africa.

A statistically significant differences on repellent usage and participant occupations was seen ($p < 0.001$) and a higher proportions of South African HCPs (88.0%; n = 125) and students (83.8%; n = 362) reported repellents usage compared to (84.6%; n = 126) and (83.4%; n = 136) from their Nigerian counterpart. However, a shift was noticed among the public respondents where a higher proprtion of the Nigerian public 87.8% (n = 43) reported using mosquito repellent compared to (64.5%; n = 91) among the South African public (Figures 3.25 and 3.26).

The repellent usage was also statistically different across the participant gender between the two contries ($p = 0.027$). More proportions of males (84.9%; n = 157) than females reported using mosquito in Nigeria. While in South Africa a reverse was seen where more females (85.0%; n = 374) reported using repellent than males (Figures 3.27 and 3.28).

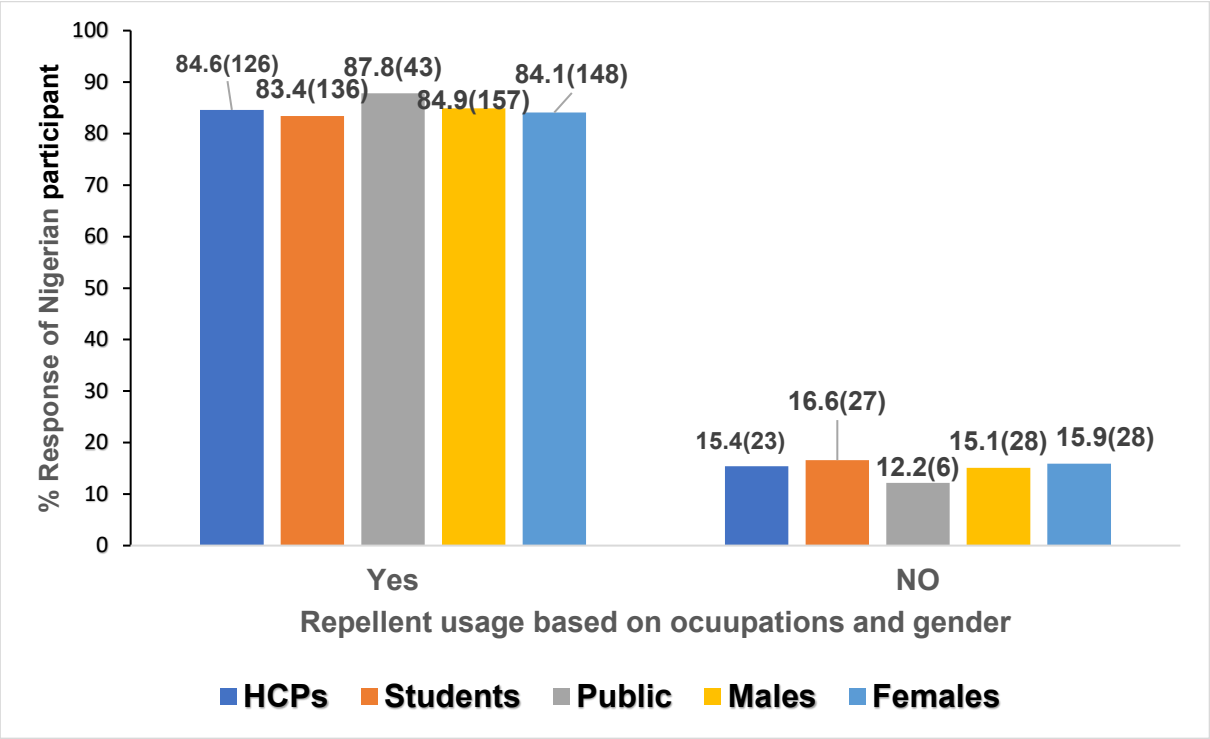


Figure 3.25: Clustered bar chart depicting the distributions of repellents use from Nigerian participants based on different occupations and gender.

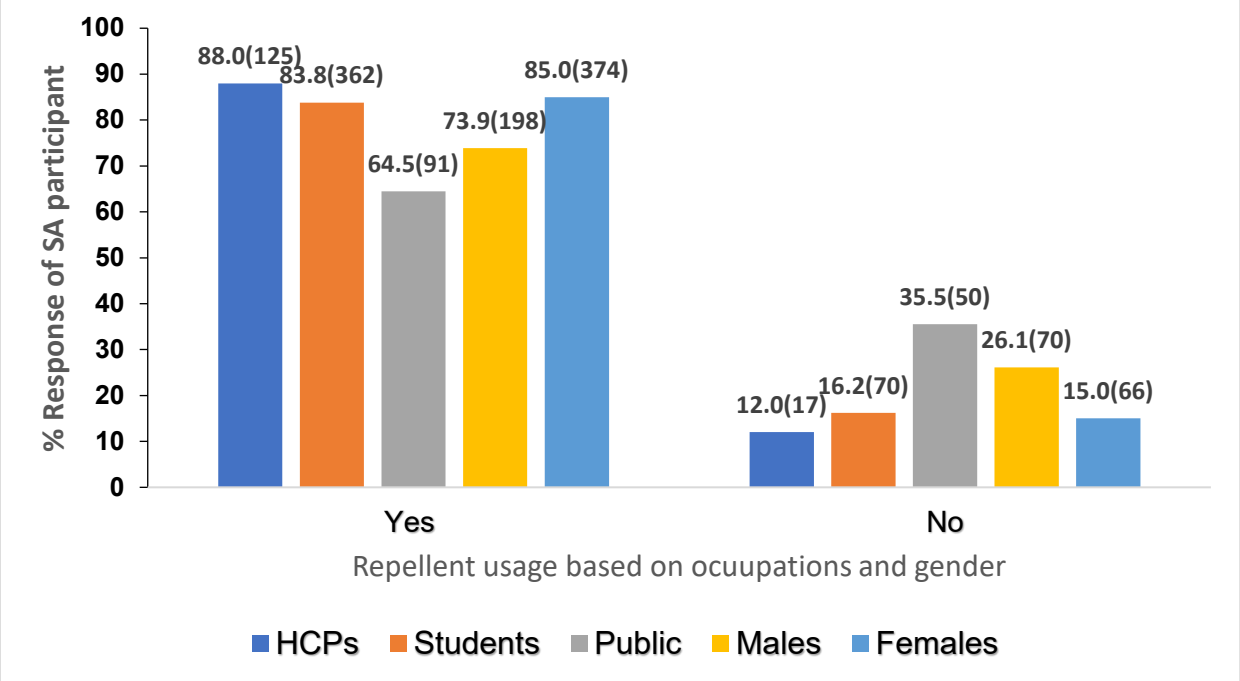


Figure 3.26: Clustered bar chart depicting the distributions of repellents use from South African participants based on different occupations and gender.

The most commonly used repellents products was Peaceful Sleep™ (62.4%; n = 469), while the least used products was No-squito™ used by (2.28%; n = 21) of the

participants (Table 3.13). With regards to the repellents side effects, overall (27.2%; n = 277) of the respondents said they have previously experienced side effects from mosquito repellents and a significantly higher proportions of Nigerians (55.0%; n = 191) reported side effects from mosquito repellents compared to (12.8%; n = 86) from South Africa ($p < 0.001$). The commonly reported repellents associated reactions such as itching and a stinging sensations experienced by (41.2%; n = 93) of the participants (Table 3.13) .

Table 3.13: Distributions of participants repellents product used and reported side effects.

Characteristics	Frequency (n)	Percentage (%)
Repellent product used		
Peaceful sleep	469	62.4
Tabard	296	39.4
Moz-free	33	4.4
No-squito	21	2.8
Raid	4	0.3
Mosquito coils	173	23.0
Morten spray	93	12.4
Citronella oil candle	3	0.3
Anti-mozzie	2	0.2
Doom	4	0.3
Vinegar	1	0.1
Burning of egg cordbox	1	0.1
Aloe water	1	0.1
Reported Side effects		
Itching and stinging sensations	93	41.2
Rashes	54	23.9
Pain	20	8.8
Other reactions	67	29.6
Can’t remember	25	11.1

3.3.5 Attitudes on prescribed antimalarial medications and commonly used antimalarial agents

Participants were asked if they have ever used antimalarial medications, a wide range of options were provided for easy identification, the options provided include: Coartem™, Quinine, Fansidar™, Artesunate, P-Alaxin, Camosunate and an option to indicate others if any of the provided options does not apply. For those that have used the antimalarial medications, they were further asked if they often completed the medications and if not to indicate the reasons for not doing so. The options provided as a reason for not completing the medications included “due to the side effects”, “I have recovered”, “do not like the medications” and “I cannot remember the reason”.

The two most used antimalarial medications reported from the total of 1,144 participants were Coartem™ (56.7%; n = 278) and Quinine™ (27.6%; n = 135); with the least used medication being Camosunate™ (7.6%; n = 37). There were more respondents from Nigeria that used Coartem™ (68.7%; n = 222) compared to (33.5%; n = 56) from South Africa, with odds that South Africans were four times less likely to use Coartem™ compared to Nigerian respondents (OR = 3.990, 95%CI = 3.150 - 5.054, P < 0.001).

However, the use of Quinine™ was higher among the respondents from South Africa with (61.7%; n = 103) compared to (9.9%; n = 32) from Nigeria, with an odd ration that almost twice as many South Africans are more likely to use quinine compared to the respondents from Nigeria (OR= 1.505, 1.100-2.060) (Table 3.14).

When asked whether they always completed the prescribed antimalarial medications, only (19.8%; n = 153) said no, while (80.2%; n = 620) said yes, they always completed the medications as prescribed. Interestingly, an equal proportion of participants from South 80.2% (n = 328) and Nigeria (80.2%; n = 292) mentioned they always completed their medications as prescribed (p = 0.993) (Figure 3.27).

Overall, the most common reason for not completing the medications was because they have recovered (40.3%; n = 60). A statistically higher proportion of Nigerians discontinue their drug because they have recovered compared to South Africans (p<0.001). There was an odds ratio that Nigerian respondents were twice as likely to discontinue their medications because they have recovered compared to South African respondents (OR = 2.192, 95%CI = 1.340 - 3.587) (Table 3.14).

Table 3.14: Commonly used antimalarial agents, Attitudes on prescribed antimalarial, Reasons for not completing the Medications and Reported Side effects

Characteristics	Overall %(n)	South Africa %(n)	Nigeria %(n)	OR (95%CI)	P value
Coartem	56.7 (278)	33.5 (56)	68.7 (222)	3.990 (3.150-5.054)	<0.001
Quinine	27.6 (135)	61.7(103)	9.9 (32)	1.505 (1.100-2.060)	0.006
Fansidar	18.2 (89)	12.0 (20)	21.4 (69)	3.088 (2.095-4.551)	<0.001
Artesunate	33.9 (166)	25.7 (43)	38.1 (123)	2.799 (2.158-3.630)	<0.001
P-alaxin	13.3 (65)	12.6 (21)	13.6 (44)	2.097 (1.471-2.989)	<0.001
Camosunate	7.6 (37)	1.8 (3)	10.5 (34)	8.345 (2.818-24.708)	<0.001
Reasons for not completing the medications					
Due to the side effects	18.1(27)	27.0 (20)	11.5 (7)	1.503 (0.630-3.585)	0.355
I have recovered	40.3(60)	37.8 (28)	52.5 (32)	2.192 (1.340-3.587)	0.001
Don't like the medications	30.2(45)	23.0 (17)	45.9 (28)	3.160 (1.751-5.701)	<0.001
I can't remember	11.4(17)	21.6 (16)	1.6 (1)		
Commonly reported side effects					
Vomiting	32.9 (98)	34.1 (46)	31.9 (52)		<0.001
Headache	22.8 (68)	28.1 (38)	18.4 (30)		0.078
Abdominal pain	10.7 (32)	17.8 (24)	4.9 (8)		0.263
Dizziness	26.5 (79)	29.6 (40)	23.9 (39)		0.003
Anorexia	10.1 (30)	8.1 (11)	11.7 (19)		0.001
Nausea	27.5 (82)	33.3 (45)	22.7 (37)		0.032
Can't remember	30.2 (90)	36.3 (49)	25.2 (41)		

3.3.6 Commonly used antimalarial chemoprophylaxis

The respondents used on three common antimalarial chemoprophylaxis approved for malaria prevention was assessed. These include: mefloquine, doxycycline and atovaquone-proguanil. The participants were asked if they have ever used any of these medications for malaria preventions, in addition to ascertain the appropriateness of the prescription in pregnancy, the female participants were further asked if they have used any of these prophylaxis during pregnancy. The most reported antimalarial prophylaxis used was doxycycline (8.0%; n = 91), while the least used antimalarial prophylaxis was atovaquone- proguanil (5.1%; n = 58) (Figure 3.27).

The antimalarial chemoprophylaxis used differs across the study countries. A statistically higher proportion of Nigerian respondents used doxycycline (11.2%; n = 44) compared to South Africans (6.3%; n = 47) with twice as many Nigerians likely to report using doxycycline for malaria prophylaxis compared to South African respondents (OR = 1.796, 95%CI = 1.213 - 2.659, p=0.003). The mefloquine (p = 0.893) and atovaquone proguanil (p = 0.051) use was not statistically difference across the two study countries (Figure 3.27).

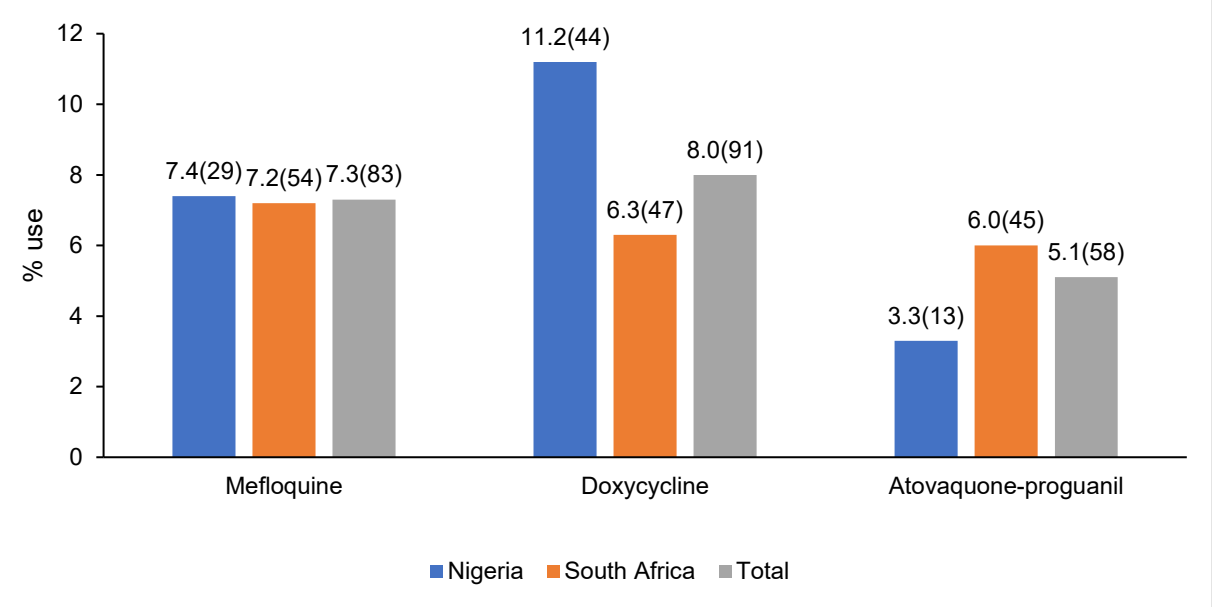


Figure 3.27: Antimalarial prophylaxis use among the study participants (total and study countries).

3.4 HCPs Knowledge on Management of Malaria

One of the objectives of this study was assessment of the knowledge of HCPs on malaria management and their adherence to the malaria treatment guidelines in their

countries. In this section the knowledge of the HCPs on the management of malaria and their adherence to the malaria treatment guidelines was analysed and compared between the two study countries.

3.4.1 Knowledge on malaria diagnosis

A series of options on commonly used malaria diagnostic methods were provided to the HCPs and they were asked to identify the methods that can be used for malaria diagnosis. The options provided include history and clinical examination, microscopy, and rapid diagnostic test (RDT).

From the total of 315 HCPs, the most known malaria diagnostic method was microscopy (74.0%; n = 233). The HCPs knowledge on malaria diagnostic methods does not differ significantly across the two countries, except for the RDT which was mentioned by higher proportions of HCPs from South Africa (78.8%; n = 119) compared to (68.9%; n = 113) from Nigeria. With an odd ratio of almost twice as many HCPs from South Africa mentioned RDT as a malaria diagnostic method compared to HCPs from Nigeria (OR = 1.678, 95%, CI = 1.006 - 2.799, P = 0.046).

The knowledge of history and clinical examination (p = 0.168), and microscopy (p = 0.395) does not differ significantly between the two countries (Figure 3.31). Out of the 315 HCPs (60.0%; n = 189) knew all the three diagnostic methods, with almost an equal proportion of HCPs from Nigeria (50.3%; n = 95) and (49.7%; n = 94) from South Africa that mentioned all the three diagnostic methods (Figure 3.28).

The knowledge of all the three malaria diagnostic methods were statistically different between the health care cadres in this study, with p values of 0.043, <0.001 and =0.001 for history and clinical examination, microscopy and RDT, respectively. The Doctors demonstrated higher knowledge on all the malaria diagnostic methods compared to other HCPs cadres (Figure 3.29).

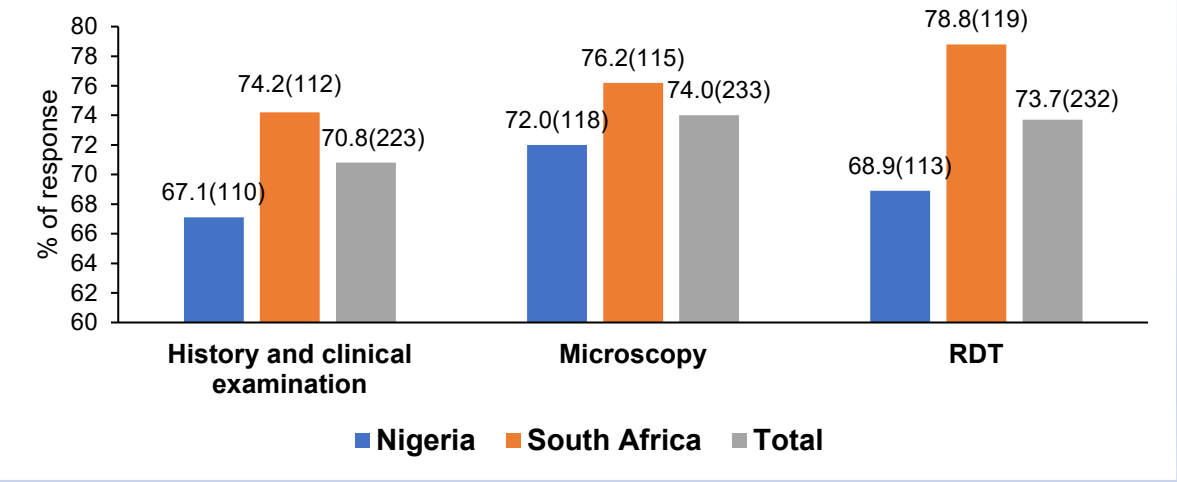


Figure 3.28: Distributions of HCPs Knowledge on Malaria Diagnostic Methods.

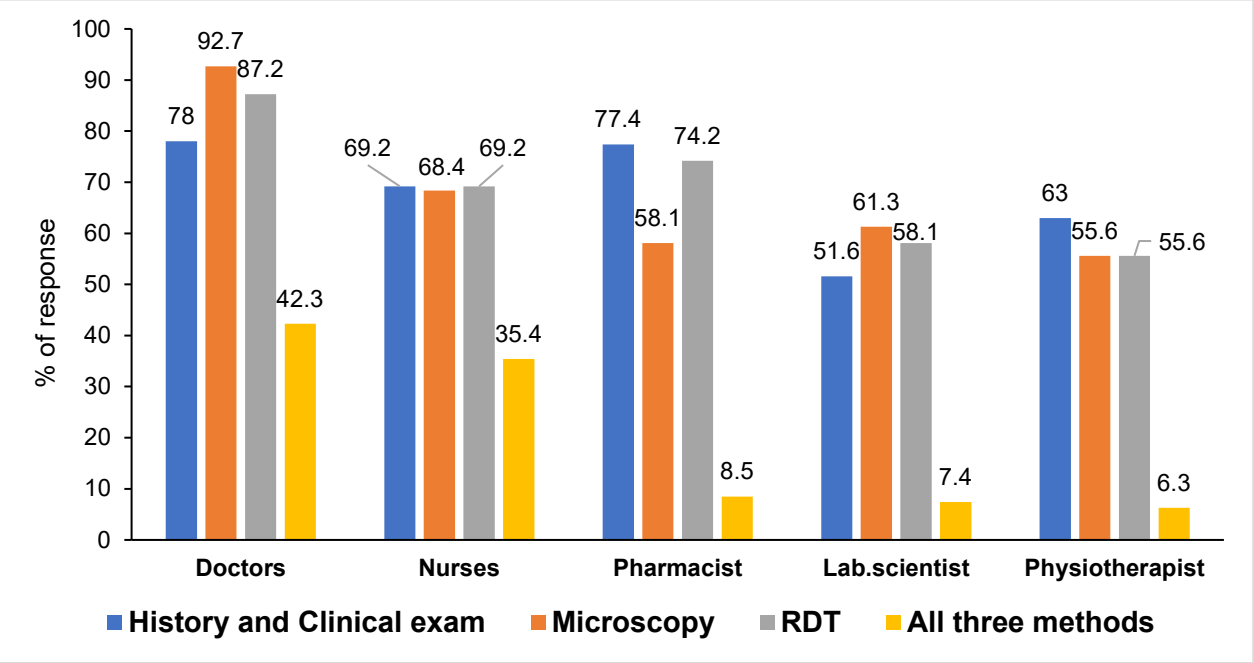


Figure 3.29: Knowledge of diagnostic methods by different HCPs occupations.

3.4.2 Knowledge on first line treatment of an uncomplicated and severe malaria

The HCPs were provided with a list of antimalarial medications and asked to identify the first line therapy approved for the management of malaria in their countries**.** Regarding the therapy of an uncomplicated malaria, the options provided include oral quinine, artemether-lumefantrine, primaquine, artesunate and mefloquine. While for the therapy of severe malaria the options provided include Intravenous (I.V) quinine, I.V artesunate, Intramuscular (I.M) artemether and I.M chloroquine.

Out of the 315 HCPs, (67.4%; n = 201) correctly identified artemether-lumefantrine as the first line therapy for an uncomplicated malaria (Figure 3.32); while (61.1%; n = 181)

correctly mentioned intravenous artesunate as the first line therapy for the treatment of severe malaria (Figure 3.30).

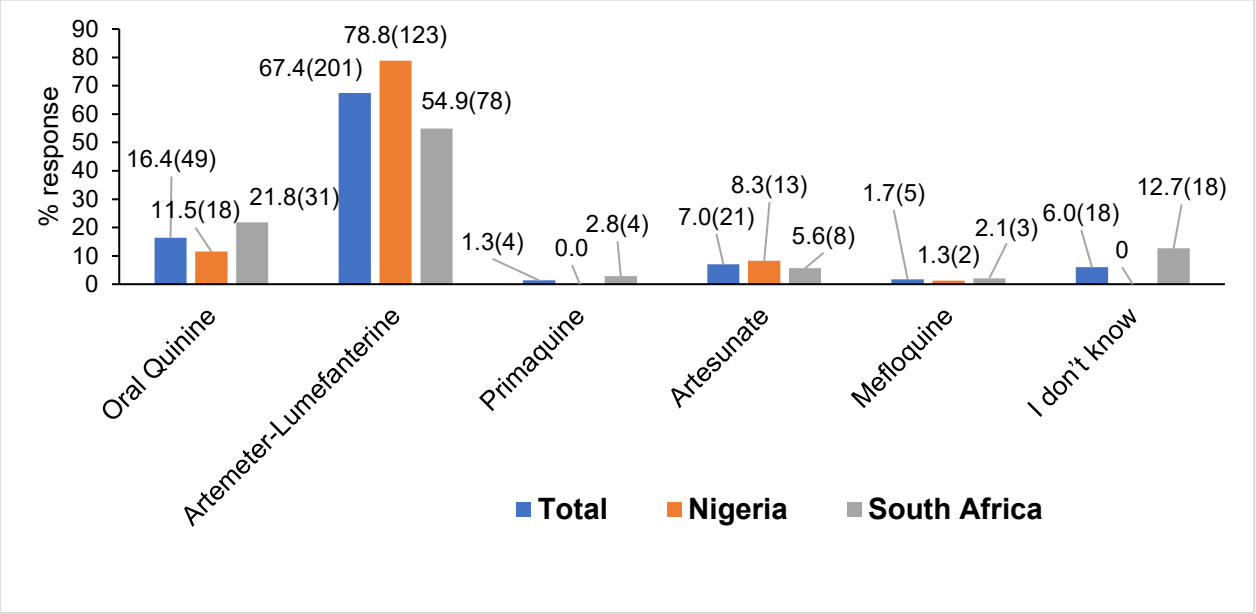


Figure 3.30: Distribution of heath care providers knowledge on the first line therapy for an uncomplicated malaria.

The HCPs knowledge of first line therapies were statistically different between the study countries with p values of < 0.001 for both uncomplicated and severe malaria. There were higher proportions of HCPs from Nigeria (78.8%; n = 123) and (66.7%; n = 104) with knowledge of an uncomplicated and severe malaria, respectively, compared to (54.9%; n = 78) and (55.0%; n = 77) for uncomplicated and severe malaria from South Africa respectively (Figure 3.31).

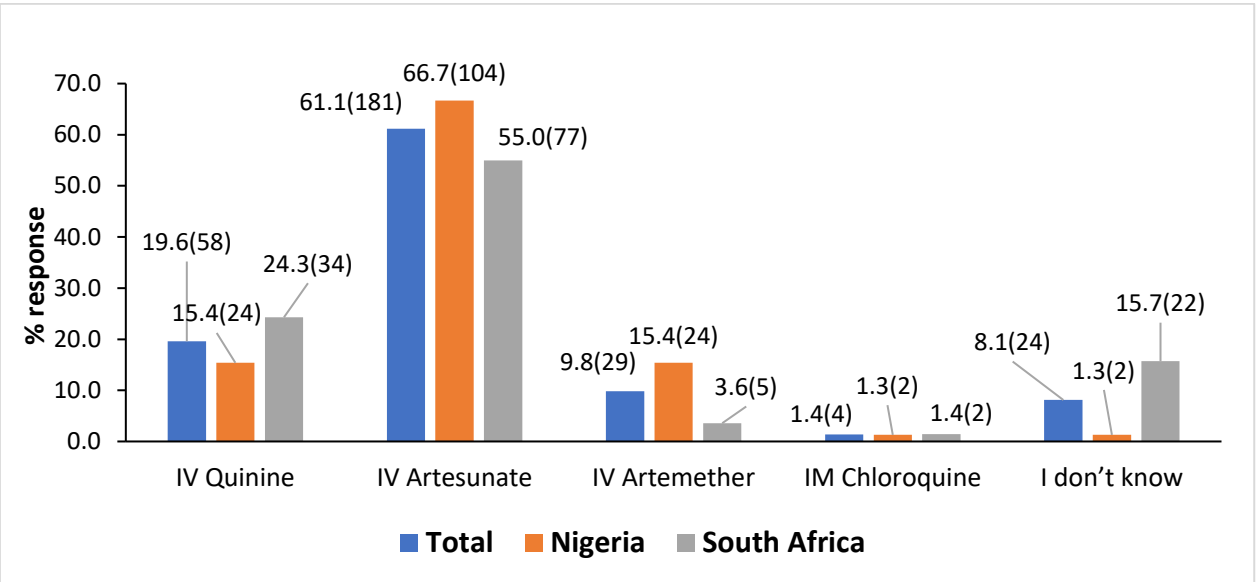


Figure 3.31: Distribution of HCPs knowledge on the first line therapy for severe malaria.

The HCPs knowledge on correct prescriptions of Coartem™ based on patients weight were statistically difference between the two countries for the patient weighing 5 to < 15kg (OR = 1.990, 95%CI = 1.383 - 2.863, p < 0.001), 15 to < 25kg (OR = 2.160, 95%CI = 1.445 - 3.230, p<0.001), 25 to < 35kg (OR = 1.907, 95%CI = 1.287 - 2.826, P = 0.001) and > 65kg (OR = 1.556, 95%CI = 1.040 - 2.327, p = 0.028) with HCPs from Nigeria having an odds of almost two times to correctly prescribed Coartem™ for an uncomplicated malaria compared to HCPs from South Africa (Figure 3.32).

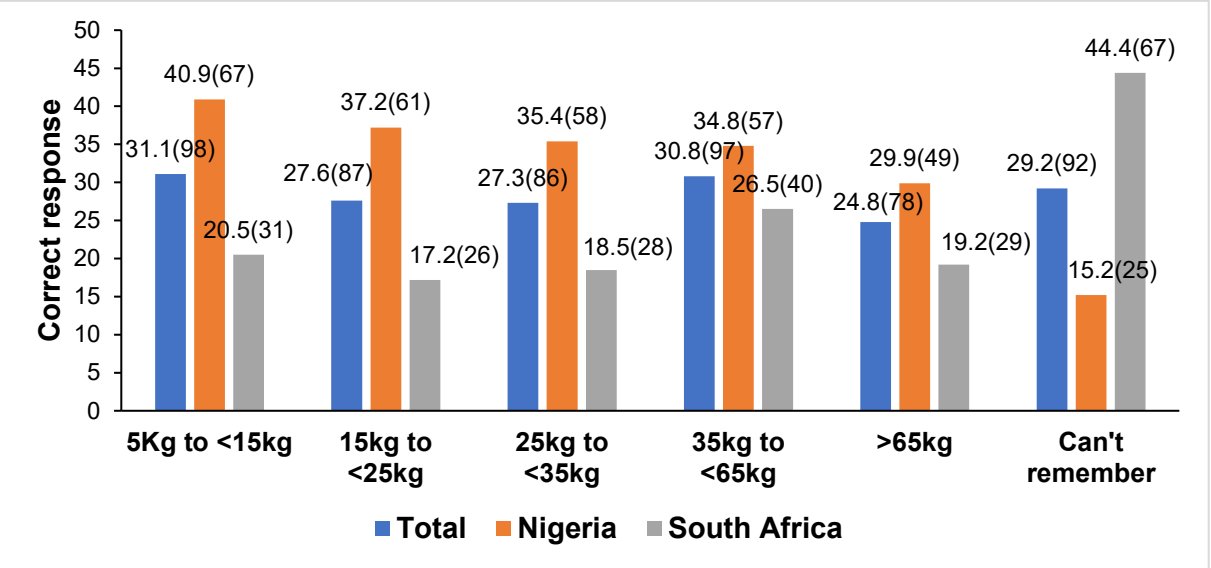


Figure 3.32: Distributions of HCPs knowledge on correct ACTs (Coartem™) regimen based on patients' weight.

For correct intravenous artesunate prescriptions for severe malaria, a shift was seen between the two countries. More correct prescriptions were obtained from South African HCPs with (12.6%; n = 19) for patient weighing > 20kg and (6.6%; n = 10) for patient weighing < 20kg, compared to (7.3%; n = 31) and (6.1%; n = 10) from Nigerian HCPs for patient weighing > 20kg and < 20kg, respectively, (p values of < 0.001 and = 0.001 for > 20kg and < 20kg, respectively) (Figure 3.33 and 3.35).

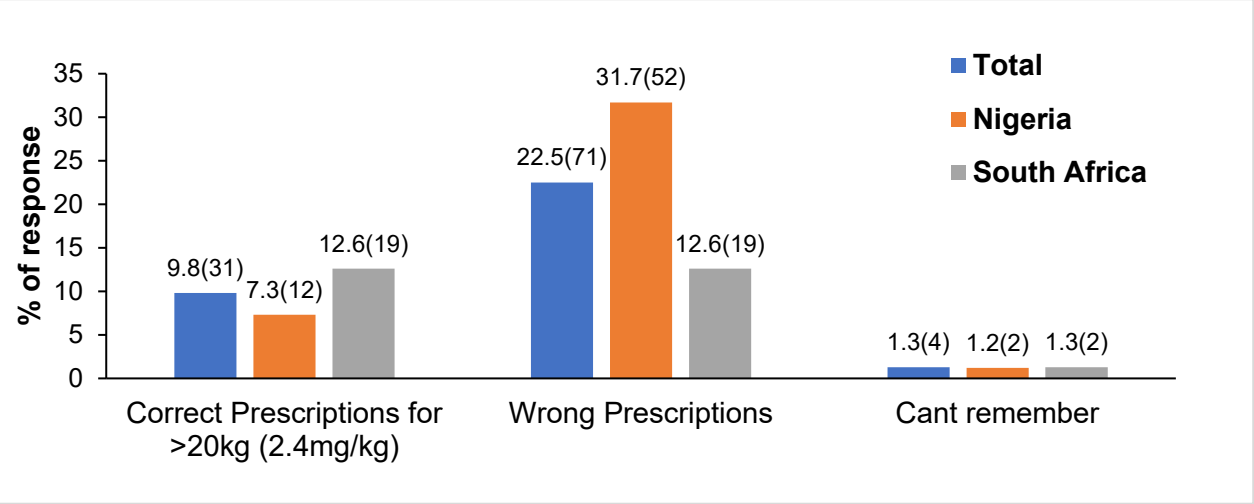


Figure 3.33: Distributions of intravenous artesunate prescriptions for severe malaria for patient weighing greater than 20kg.

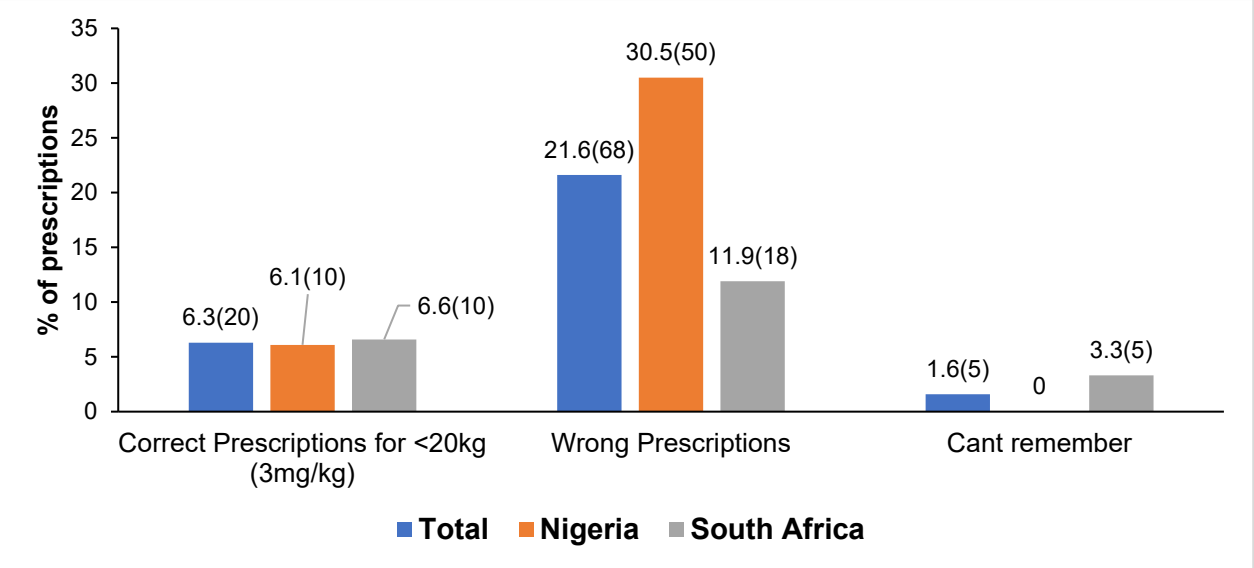


Figure 3.34: Distributions of intravenous artesunate prescriptions for severe malaria for patient less than 20kg.

For the preferred medications for management of severe malaria based on personal preference from years of clinical experience a statistically significant differences were noticed between the two countries ($p < 0.001$). A higher proportion of HCPs from Nigeria preferred the approved medication (artesunate) (69.8%; n = 97) compared to those from South Africa (54.5%; n = 73) (Figure 3.35).

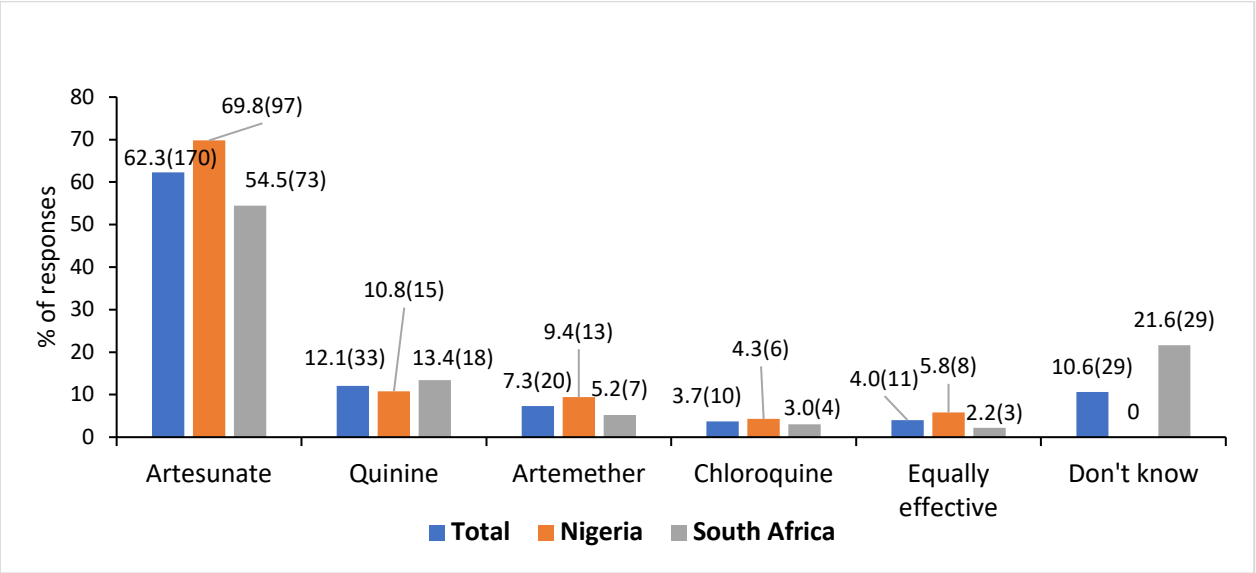


Figure 3.35: Distributions of HCPs prepared medications for the management of severe malaria based on clinical experience.

3.4.3 HCPs knowledge on the correct regimen for antimalarial prophylaxis medications

The HCPs participants were provided with a series of questions about the antimalarial prophylaxis to ascertain their basic knowledge on the chemoprophylaxis for malaria prevention and the prescriptions regimen based on the current Nigerian and South African malaria prevention guideline (SADOH, 2018; CDC, 2021). Regarding the nationally approved antimalarial prophylaxis six options were provided which included: doxycycline, artesunate, atovaquone-proguanil, artemether-lumefantrine, mefloquine and quinine. They were also asked about the recommended prophylactic regimens of the approved medications and which of the approved medications can be or cannot be used in pregnancy.

Mefloquine has a set of contraindications that need to be considered before it can be prescribed, these contraindications include history of epilepsy or psychiatric illness, past severe reactions to mefloquine, infant weighing less than five kilograms and underlying cardiac disturbances or arrhythmias (SADOH, 2018; CDC, 2021), the HCPs knowledge on these contra indications related to the use of mefloquine were also assessed.

Among the total of 315 HCPs, the most known antimalarial prophylaxis was atovaquone-proguanil (34.3%; n = 108). The most known malaria chemoprophylaxis

among the South African HCPs was doxycycline (57.6%; n = 87), while atovaquone-proguanil (22.6%; n = 37) was the most known chemoprophylaxis among the HCPs from Nigeria. A statistically higher proportions of HCPs from South Africa demonstrated good knowledge on malaria chemoprophylaxis compared to HCPs from Nigeria. The p values were < 0.001 on all the three chemoprophylaxis. The HCPs from South Africa were three to 23 times more likely to mention malaria chemoprophylaxis compared to HCPs from Nigeria. Also, only (1.8%; n = 3) HCPs from Nigeria mentioned all the three-malaria chemoprophylaxis compared to (23.8%; n = 36) from South Africa (Table 3.15).

Table 3.15: Knowledge of HCPs on antimalarial prophylaxis across the study countries.

Prophylaxis	Total %(n)	Nigeria %(n)	South Africa %(n)	OR (95%CI)	P values
Doxycycline	30.5 (96)	5.5(9)	57.6 (87)	23.411 (11.109-49.340)	<0.001
Atovaquone-Proguanil	34.3 (108)	22.6 (37)	47.0 (71)	3.046 (1.874-4.953)	<0.001
Mefloquine	29.8 (94)	11.6 (19)	49.7 (75)	7.531 (4.239-13.382)	<0.001
Mentioned all three	12.4 (39)	1.8(3)	23.8 (36)	16.800 (5.051-55.882)	<0.001

With regards to the correct regiments of malaria chemoprophylaxis, there was still a statistically higher proportion of South African HCPs demonstrating good knowledge on prophylaxis regimen of all the three medications compared to HCPS from Nigeria viz: doxycycline (OR=4.954, 95%CI=2.714-9.042, p<0.001), Mefloquine (OR=2.203, 95% CI=1.385-3.502, p=0.001) and atovaquone-proguanil (OR=3.071, 95%CI= 1.849-5.102). These data indicated that the South Africans were two to four times more likely to give a correct regimen of malaria chemoprophylaxis compared to HCPs from Nigeria (Figure 3.36). Furthermore, a statistically higher proportions of HCPs from South Africa demonstrated good knowledge on contraindications to the use of mefloquine compared to those from Nigeria (p<0.001) (Figure 3.37).

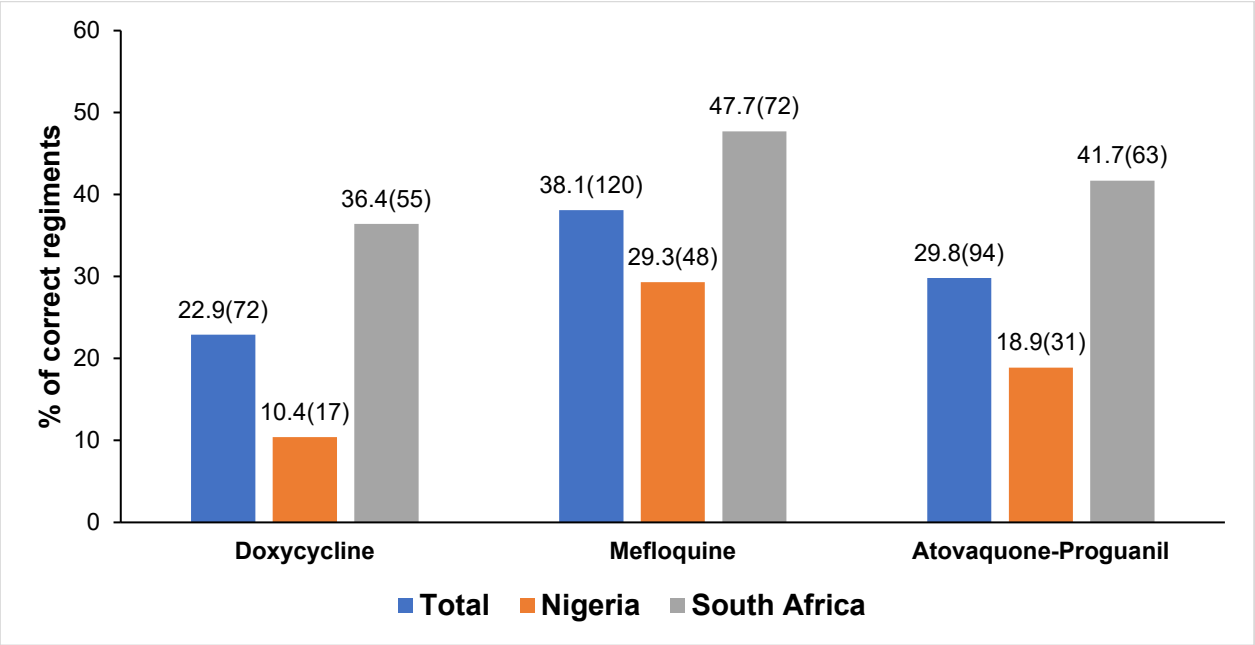


Figure 3.36: Distributions of the HCPs correct prescriptions regimen of an antimalarial chemoprophylaxis

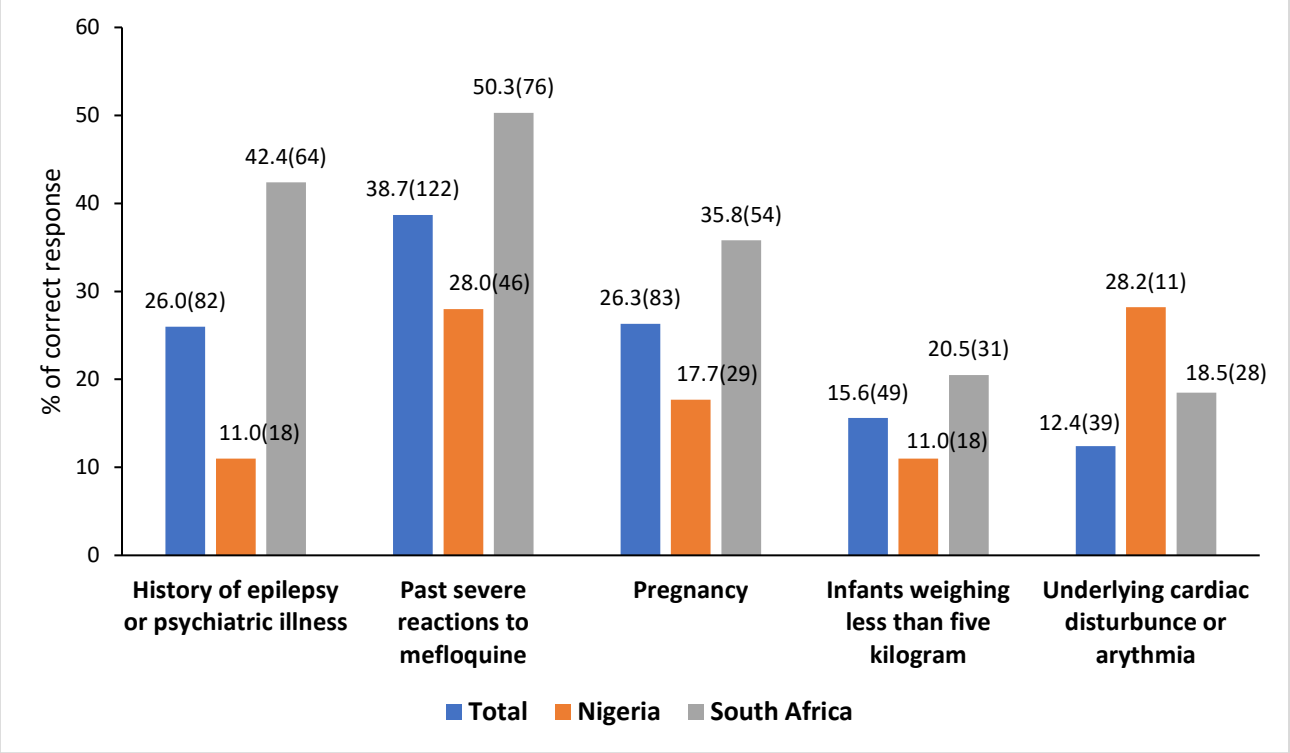


Figure 3.37: HCPs knowledge on the different contraindications to the use of mefloquine.

3.4.4 Assessment of the HCPs sharing of malaria-related information

Out of the 315 HCPs, (72.9%; n = 199) said they always educated their malaria positive patients on malaria-related information; with a statistically higher proportion of HCPs

from Nigeria (81.9%; n = 118) reporting that they educate their patients compared to 62.8%; n = 81 from South Africa ($p < 0.001$) (Figure 3.38).

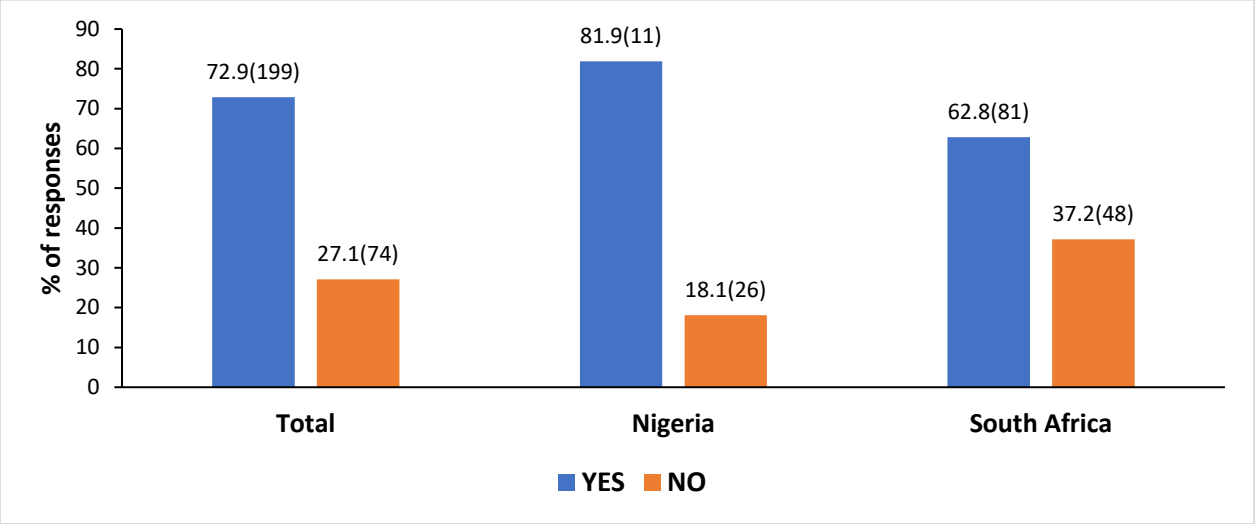


Figure 3.38: Distributions of malaria-related information sharing by HCPs across the study countries.

The two most common information shared by the HCPs were uncomplicated malaria positive patient to return to the hospital at any time if deteriorating (45.1%; n = 142) and adherence to medications (44.8%; n = 141) (Figure 3.39).

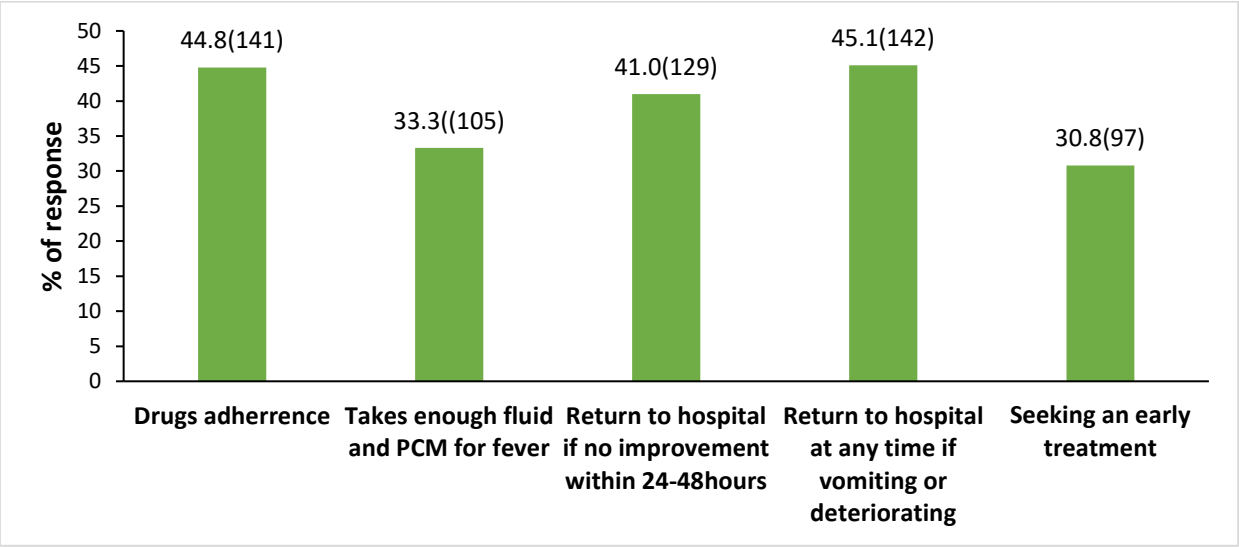


Figure 3.39: Types of malaria-related information shared by HCPs.

3.5 Market and Online Survey

3.5.1 List of mosquito repellents obtained from the market and online survey

An online and market surveys were conducted to ascertain and document the different insect repellent products that were available in Johannesburg, South Africa. The market survey was conducted in mall, pharmacies, street stalls, warehouses, and supermarkets within Johannesburg, as well as an online search using three different search engines. A total of 92 different repellent products were documented (Table 3.16), including (22.8%; n = 21) from the market survey (Table 3.17) and (77.2%; n = 71) from an online search. The cost of these repellents ranged from a minimum of R12.49 to a maximum of R1,252.57 with a median cost of R99.00 (IQR= R52.21-R621.10). ANOVA test indicated a statistically significant differences between the means of the market and online cost of the repellents ($p < 0.001$). Only (59.8%; n = 55) of the surveyed products were approved in South Africa, while the certification of (40.2%; n = 37) of the products were not specified.

3.5.2 Active ingredients of the surveyed repellent products

The commonly found active ingredient was citronella oil (33.3%; n = 32), followed by lemon grass oil (16.7%; n = 16) with DEET found in only (7.3%; n = 7) of the products. For some of the products the active ingredients were not specified and (28.1%; n = 27) were said to contain natural plant products. A total of (13.5%; n = 13) products were electrically powered that used either ultraviolent light or sound waves (Figure 3.40).

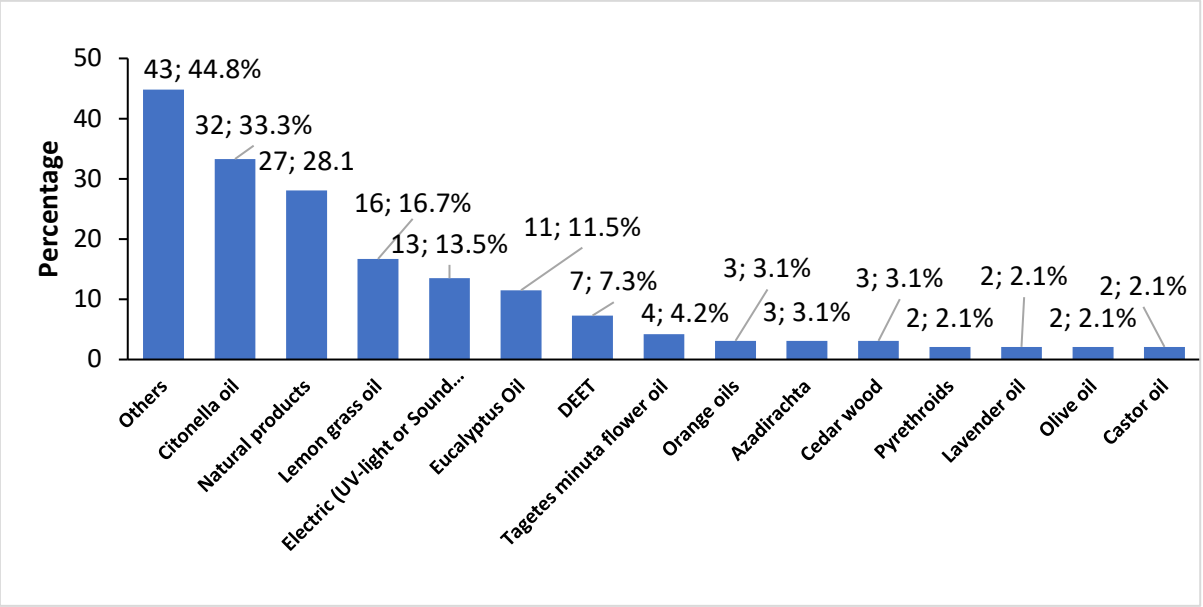


Figure 3.40: Active ingredients found in the survey repellent products.

Table 3.16: Repellents/ insecticide products obtained from an online survey.

S/N	Name	Manufacturer/ Supplier	Ingredients & Duration of Action	Cost (Rand)	Repellent Image	Certification in S.A	Reference
SYNTHETIC PRODUCTS							
1	Doom -Destroyer Mosquito Room Spray	Tiger Consumer Brands	D-Phenothrin (Pyrethroid) 0.92 g/kg, Imiprothrin (Pyrethroid) 0.25 g/kg, Prallethrin (ETOC) (Pyrethroid) 0.4 g/kg,	33.99		Yes	Clicks+, 2020a
2	Mortein-Multi Insect Killer	Reckitt Benckiser South Africa	Allethrin (2.09 g/kg) and Resmethrin (0.39 g/kg)	27.99		Yes	Clicks+, 2020b
3	Peaceful Sleep Mosquito Room Spray	Tiger Consumer Brands Limited.	DEET 8 hours	46.99		Yes	Clickss+, 2020d
4	W4W Mosquito Repellent Coils - Stands)	Ubuy	Pyrethroid	335		Yes	UBUY, 2020c
5	Repel Permethrin Clothing & Gear Insect Repellent	Repel	Permethrin Up to 4 weeks	248		Yes	REPEL, 2020b
6	Repel Sportsmen Max Aerosol Insect Repellent	Repel	DEET	568		Yes	REPEL, 2020c
7	Robosol Auto Insect Control	Takealot	Pyrethrum	989.00		Not specified	Takealot, 2020b
8	Sawyer Products Premium Insect Repellent	Ubuy	Picaridin	260		Yes	UBUY, 2020b

9	Smart Voetsek Fly Repellent	Midfeed Stack 'n Togs	DEET, *Targetes* and Eucalyptus	1252.57		Yes	Mid Feedstack 'N Togs, 2020
10	Tabard Fabric guard insect repellent	Tabard	Permethrin			Yes	Tabard, 2020
NATURAL PRODUCTS							
S/N	Name	Manufacturer/Supplier	Ingredients & Duration of Action	Cost (Rand)	Repellent Image	Certification in S.A	Reference
1	Ananta Luxury Hand Rolled Incense - Citronella	Faithful to Nature	Citronella, Natural Gums, Resins, Herbs, Spices, Essential Oils	39.50		Not specified	Faithful to Nature, 2020a
2	Badger Anti Bug Balm Travel Size	Faithful to Nature	Citronella, Pelargonim, *Cedrus Atlantica* (Cedar), Lemongrass,Rosemary,, Geranium.	125.00		Yes	Faithful to Nature, 2020b
3	Biogrow Bioneem insect repellent	Faithful to Nature	1500ppm Azadirachtin.	195.00		Not specified	Faithful to Nature, 2020
4	Biogrow Vegol Organic Insecticide	Faithful to Nature	Canola oil, Emulsifier.	101.00		Not specified	Faithful to Nature, 2020e

5	Bugger Off Body Spray	Cape Union Mart	*Tagetes* oil	75.00		Not specified	(CapeUnionmart, 2020a)
6	Bugger Off Soap 100g	Cape Union Mart	Natural glycerine product	35.00		Not specified	(CapeUnionMart, 2020b)
7	Citro Lotion 125ml	Dischem Pharmacy	Citronella	52.95		Yes	(DISCHEMPHARMACY, 2020b)
8	Citro-cream	Dischem Pharmacy	Cironella Oil and Lemon Grass	37.95		Yes	(DISCHEMPHARMACY, 2020a)
9	Coghlan's Citronella Candle	Outdoor Warehouse	Citronella	115.00		Yes	OutDoor Ware, 2020a
10	Dis-Chem Citronella Oil 20ml	Dischem Pharmacy	CITRONELLA	26.95		Yes	(DISCHEMPHARMACY, 2020c)
11	Earthsap Bugs Away Roll-On	Faithful to Nature	Grapeseed/ soybean oil, vegetable, glycerine, mint oil, lemongrass oil, citronella, oil, camphor oil, clove oil and eucalyptus oil.	50.00		Yes	Faithful to Nature, 2020f
12	EFEKTO -100ml mole repellent	Game	Natural plant products	149.99		Yes	Game, 2020a

13	Essentially Natural Citronella Oil	Essentially Natural	Citronella	39.00		Yes	Essentially Natural, 2020b
14	ever Tree Fly and Mosquito Repellent 250g	OutDoor Warehouse	Natural oil products	99.00		Yes	OutDoor Warehouse, 2020b
15	Greenerways Organic Insect Repellent	Ubuy	Natural products	494.00		Not specified	UBUY, 2020a
16	Greenerways Organic Mosquito Repellent Zone - New Improved Formula	Greenerways Organic	Natural products	514.00		Not specified	Greener Ways Organic, 2020
17	HHL Vital Protection	Cape Union Mart	Natural products	125.00		Not specified	Cape Union Mart, 2020b
18	Essentially Natural Bug Off! Insect Repellent	Essentially Natural	Cedarwood oil, Citronella oil, Eucalyptus oil, Grape Seed oil, Lemongrass oil, Peppermint oil.	69.00		Yes	Essentially Natural, 2020a
19	Just Pure Natural Insect Repellent	Faithful to Nature	rose geranium, Aqua, sesame oil, essential oils of Cedarwood, lime, sorbitol, alcohol.	136.00		Not specified	Faithful to Nature, 2020g
20	KiddieKix Bugz Off Insect Repellent	Faithful to Nature	lemongrass, Rose,, cedarwood, smithi , geranium and L*ippia javanica* and eucalyptus,	80.00		Not specified	Faithful to Nature, 2020h

21	Lifetrek Mosquito Band Kids	OutDoor Warehouse	Natural Products 6hours.	79.00		Not specified	OutDoor Warehouse, 2020d
22	Mortein Natural Guard Insect Control System	Reckitt Benckiser	Citronella 4 weeks	98.99		Yes	Clicks+, 2020c
23	Mosquito Guard Repellent Stickers/ Patches for Kids	Modern Day Products	Rosemary, Peppermint, Citronella, Lemongrass, and essential oils.	387		Not specified	Modern Day Product, 2020
24	Mosquito repellent cream	Proguard Natura	Natural Products	64.99		Not specified	Proguard Natura, 2020
25	Mosquito repellent spray	Proguard Natura	Natural Products	74.99		Not specified	Proguard Natura, 2020
26	Murphy's Naturals Mosquito Repellent Sticks	Murphy's Naturals Inc.	Citronella, Rosemary, Cedarwood, Lemongrass, Essential Oils, Peppermint and Bamboo	256.00		Yes	Murphy's Naturals, 2020
27	Natural Orange Household Insect Repellent	Faithful to Nature	Aqua, Eucalyptus Oil, Orange Oil, Lemongrass Oil and Emulsifier	106.00		Not specified	Faithful to Nature, 2020i
28	No-Bite-Me Soap and Creme	Pc link computers	All-natural products	913.00		Yes	PCLinksComputers, 2020

29	Onguard Pump Spray 150ml	Avid Brands	*Chyrysanthenum Cinaeriafolium* and *Azadirachta*	69.00		Not specified	AVIDBRANDS, 2020
30	Pannatural Pets Anti-Bug Spray	Faithful to Nature	Citronella Oil, Vegetable,Eucalyptus Oil, Sunflower Oil,Glycerine,*Tagetes minuta,* Lemongrass Oil, *and* Peppermint Oil	70.00		Yes	Faithful to Nature, 2020k
31	Pigeon Anti Mosquito Baby Wipes	Dischem Pharmacy	Natural products	59.95		Not specified	(DISCHEMPHARMACY, 2020e)
32	Purity & Elizabeth Anne's Baby Insect Repellent Cream	Dischem Pharmacy	Natural products	49.95		Not specified	(DISCHEMPHARMACY, 2020f)
33	Purity & Elizabeth Anne's Baby Insect Repellent Spray	Dischem Pharmacy	Natural products	59.95		Not specified	(DISCHEMPHARMACY, 2020g)
34	Reitzer Camp/Outdoor Soap	Takealot	Glycerine and Citronella	47,00		Yes	Takealot, 2020a
35	Rep.Umbrella - Citronella Oil 1.5L	Game	Citronella	149.00		Yes	Game, 2020d
36	Repel Lemon AEROSOL Eucalyptus Insect Repellent	Repel	Eucalyptus	625		Not specified	REPEL, 2020a

37	Republic Umbrella Citronella Mosquito Repellant Candle	OutDoor Warehouse	Citronella	89.00		Yes	OutDoor Warehouse, 2020e
38	Republic Umbrella Citronella Table Lamp	OutDoor Warehouse	Citronella	169.00		Yes	OutDoor Warehouse 2020f
39	Republic Umbrella Mosquito Guard	DISCHEM PHARMACY	Natural products 5hours	59.95		Yes	DISCHEMPHARMACY, 2020e
40	Riddex Plant Seeds Mosquito Repelling Grass	NewChic	Riddex plant Grass	72.17		Not specified	Newchic, 2020
41	Sea to Summit Citronella	Cape Union Mart	Citronella	99.00		Yes	(CapeUnionMart, 2020b)
42	Soylites Coconut Candle Insect repellent blend	Faithful to Nature	Coconut, non-toxic fragranced candle, and vegetable wax,	165.00		Not specified	Faithful to Nature, 2020l
43	Tabard Candle Small 120g/240g	OutDoor Warehouse	Citronella	69.00		Yes	OutDoor Warehouse, 2020h
44	Tabard Citronella Night Lights 18'S	Acron Group	Citronella	169.99		Yes	Clicks+, 2020f

45	Tabard Stick 30ml	OutDoor Warehouse	DEET	69.00		Yes	OutDoor Warehouse, 2020i
46	Wild Basil & Lemongrass Mosquito Repellent	Faithful to Nature	Botanical extracts of African basil, lemongrass Thyme, Camphor, *Litsea cubena* and Lavender	180.00		Yes	Faithful to Nature, 2020
No	**Name**	**Manufacturer/ Supplier**	**Ingredients & Duration of Action**	**Cost Rand**	**Repellent Image**	**Certification in S.A**	**Reference**
ELECTRONICS PRODUCTS							
1	Elektra Anti Mozz Lamp	Dischem Pharmacy	UV Light	309.95		Not specified	(DISCHEMPHARMACY, 2020d)
2	Fever Tree Non-Toxic Liquid Plug-in Combo Pack	OutDoor Warehouse	Natural Products	199.00		Not specified	OutDoor Warehouse, 2020c
3	HOMEMARK Ultrasonic Insect Repeller	Game	UV Light	299.00		Not specified	Game, 2020b
4	LED Mosquito Repellent Globe	Future Light	Produces a wavelength of light disliked by mosquitos and other insects.	139.00		Not specified	Future Light, 2019
5	Leisure quip - usb rechargeable mosquito killer with led light	Game	UV Light	299.99		Not specified	Game, 2020c

6	New Intelligent Ultrasound Artifact Mosquito Repellent	Light In the Box	Ultra-sonic sound	161.87		Not specified	Light In The Box, 2019
7	Non-Toxic UV Mosquito Killer Lamp Insect Trap	Gearbest	Non-Toxic UV light	284.46		Not specified	Gearbest, 2014
8	Radius Zone Mosquito Repellent	Want-it-all	UV light	1 965		Not specified	Wantitall, 2020
9	Raid Electric Diffuser	SC Johnson & Son	Transfluthrin	44.99		Yes	Clicks+, 2020e
10	Sothing Cactus Mosquito Killer and Repellent	Makro	360° UV Violet Light	599		Not specified	Makro, 2019
11	Ugreen USB powered Mosquito Repellent	Loot	Electric Mosquito Killer	105		Not specified	Loot, 2019
12	Ultrasonic Mosquito Repellent Bracelets	Bluetooth Mouse Tech	UV light	457.32		Not specified	Bluetoothmousetech, 2020
13	Ultrasonic Mosquito Repellent	Newchich	Multi frequency Ultrasonic sound	235.19		Not specified	Newchic, 2019
14	USB Charging Electric mosquito Repellent	Banggood	Electric Mosquito Repellent	162.21		Not specified	Banggood, 2006
15	UV Light Pest Repeller	Banggood	Ultra-violent light	106.26		Not specified	Banggood, 2018

Table 3.17: Repellent products obtained from the market survey.

Name	Ingredients	Method of Application	Manufacturer	Approval
MOZ- FREE Mosquito Repellents	Petrolatum, Lemon grass oil, *Tagetes minut*a Flower oil, Eucalyptus Globulus Leaf oil, and Citronella oil.	To be applied lightly on the skin.	COMAFRICA Products of South Africa	Yes
No Squito Lotion	Plant oils, Nut oils, and Orange oils.	DEET free to be applied all over the body as frequently as needed	G &R traders in South Africa.	Yes
Tabard.	Each 1g contains 195mg of diethyltoluamide DEET)	Apply lightly, evenly, and completely to all exposed skin, except eyes and mouth.	Acorn products	Yes.
Peaceful Sleep cream	Each 1,0 g cream contains Diethyltoluamide 250,0 mg	Apply frequently to the entire area of the skin to be protected, do not apply to the mouth, eyes and hands of young children.	Tiger Consumer Brands Limited.	Yes
Peaceful Sleep stick	DEET 10.5g	Apply lightly to exposed skin	Adcock Ingram	Yes
Mortein power Gard liquid (electrical gadget)	20.15g/l d-trans Allethrin75/25 pyrethroid)	To be plug to the source of electricity.	Reckitt Benckiser South Africa	Yes
Citronella candle	Paraffin, Citronella	To be placed on a heat resistant surface before lighting the candle	Klicks+	Yes
All natural NGUARD insect repellent cream	Each 150mls container contains 750mg of *Chrysanthenium cineriaefolium* extract and 6900mg of *Azadirachta indica* seed extract.	To be apply on the whole skin. Including infant	Avid Brand SA	Yes
Anti-Mozzie cream	Citronella and lemon grass oils	To be apply to the skin as often as required	Reitzer pharmaceuticals	Yes

Mosquito guard cream	Oil of lemon eucalyptus extract	Apply all over the skin	Republic-umbrella in SA	Yes
Name	**Ingredients**	**Method of Application**	**Manufacturer**	**Approval**
MEDIC insect repellent cream	Citronella oil	Apply to the exposed skin when necessary.	Medic + self-care	Yes
Mosquito spray	Water, natural extracts, flavourist and sodium benzoate	Shake bottle well and spray on the skin and hair	So pure Naturally	Yes
No fly repellent	Citronella oil	Two candle per pack for lightning	No Fly candles cc	Yes
Bennett's Mozzie stick	Citronella oil, hydrogenated Castor oil, Lavender oil, Lemon grass oil, *Zinzib*a oil,	Apply to the skin, mainly for babies	Bennetts Brothers cc	Yes
Pure beginning spray	Citronella, lemon bush, eucalyptus neem and lemon	Shake and spray to the exposed body areas	Pure beginning	Yes
Mylol perfumed mosquito repellent stick	Citronella oil, *Cymbopogon nardus*, propylene glycol, sodium metabisulphate.	Apply lightly on exposed body surface including face.	Rolfe laboratories	Yes
Mosquito patch	Citronella oil 15%m/m	Attach the adhesive patch to your cloths and nearby locations	Life Trek	Yes
Clicks Citronella kids wipe	Aqua, citronella oil, *Cedrus deodra* oil, menthol, etc	Use wipe over exposed areas, avoid face	Clicks group	Yes
Mosquito band anti-insect repellent	Citronella oil 0.75g/band	To be worn on the wrist to repell mosquitoes and insects	Life Trek	Yes
Tabard citronella candle	Citronella oil 50g/kg	Place on non-combustible surface before lightning	Acorn products	Yes
Portable ultrasonic repellent	It emits 5-20 multi frequency sound waves that repel mosquitoes of different species	Press the white button once for 4 hours, twice for 6 hours, three times for 12 hours protection.	Life Trek	Yes

3.6 Efficacy of Commercially Available Mosquito Repellents in Johannesburg, South Africa

An efficacy assays were conducted for fifteen repellents to ascertain the percentage of their protection from mosquito bites (Table 3.18). The repellents efficacy assays were only conducted in South Africa due to the lack of a working malaria insectary in Birnin Kebbi metropolis, Kebbi State, Nigeria. This makes it impossible to breed the mosquitoes and get nulliparous female *Anopheles gambiae* mosquitoes of uniform age, specifically 5 to 8 days as recommended in WHO repellent assays guideline (WHO, 2013) for comparison with South African assays and other similar studies.

Table 3.18: Repellent products tested, active ingredients and products concentrations.

Product name	Active Ingredients	Concentrations
Tabard	DEET	Each 1g contains 195mg of diethyltoluamide DEET)
Citro-bar Soap	Citronella oil only	Not specified
Life Trek, Mosquito Spray	IR3535	Not specified
Medi Scabiol Soap	Citronella oil only	Not specified
Mosquito guard	PMD Citriodiol)	Not specified
Anti-mozzie camping, outdoor and indoor cream	Citronella oil plus other plants extracts	Not specified
No-squito lotion	Other plants extract without citronella	Not specified
Pure Beginning Organic Care, 100% Natural Insect Repellents.	Citronella oil plus other plants extracts	Not specified
Medic Insect Repellent Cream	Citronella oil only	Not specified
All-natural guard insect repellent	Other plants extract without citronella	750mg *Chrysanthemum cineriae folium* extract, 6900mg *Azadirahta indica* extract.
So Pure Naturally, Mosquito Spray.	Other plants extract without citronella	Citronella oil 150g/kg per patch
Moz-free mosquito repellents	Citronella oil plus other plants extracts	Not specified
Mylol perfumed mosquito repellent	Citronella oil plus other plants extracts	Not specified
Mosquito Patch Insect Repellents	Citronella oil only	Not specified
Bennet's, Mozzie stick	Citronella oil plus other plants extracts	Not specified

3.6.1 Demographics of volunteers

For Part two of this study, the repellent efficacy test, nine volunteers were used for the whole experiment that included 5 males (55.6%) and 4 females (44.4%). A total of 60 assays were conducted, four replicates each for the 15 repellents tested (240 replicates). Out of these 60 assays, 80.0% (n = 48) were performed by the male volunteers, while (20.0%; n = 12) were performed by the female volunteers, however this difference was not statistically different ($p = 0.172$). The mean age of the volunteers for the repellent efficacy assays was 33.60 ± 4.55 years, with relatively older males (mean 34.96 ± 01.60 years) than females (28.17 ± 7.74 years) ($p < 0.001$).

3.6.2 Repellent products tested and their active ingredients

Out of the fifteen tested insect repellents, (33.3%; n = 5) contained citronella oil plus other plants extracts, (26.7%; n = 4) contained only citronella oil, (20%; n = 3) contained other plants extracts without citronella, (6.7%; n = 1) contained DEET, (6.7%; n = 1) contained IR3535, while (6.7%; n = 1) contained PMD as the active ingredients (Table 3.18 above).

3.6.3 Percentage attractions and repellency

Percentage attraction is the determinant of the spatial repellence activity of an insect repellent product, a good repellence activity is indicated by the lower percentage attraction. It was calculated by dividing the average number of mosquitoes counted at the treated arm net divided by the total number of mosquitoes used for the test, minus any damaged mosquito (WHO, 2013).

The average number of the mosquitoes on the treated arm net were obtained by calculating the mean of the number of mosquitoes counted on the treated arm over an hour at interval of 15 minutes and for all the four volunteers (See Equation 2.2 in Chapter two), while the percentage protection was accordingly calculated (Equation 2.3).

Out of the 15 repellents that were tested, the medi-scabiol soap provided the highest level of protections 99.45 ± 0.28), it is a citronella-based insect repellent, and it provided an individual protection of 99.78%, 99.49%, 99.44% and 99.10% for the first, second, third and fourth volunteers respectively **(Table 3.19).** The knockdown effects were noted only by the two repellent products tested, viz: Pure Beginning, and Moz-Free mosquito repellents, both provided a knockdown effect of 5% (n = 1/20).

Table 3.19: Showing the percentage repellency of the tested repellents products.

Product Name	Volunteers	Average number of mosquitoes on the Control Arm net C)	Average number of mosquitoes on the Treated Arm net T)	% Repellency $(C * t - T)/(C * t) * 100$
Tabard	V1	1.75	0.00	100.00
	V2	2.50	2.00	98.67
	V3	2.25	2.50	98.15
	V4	3.00	0.50	99.72
	Mean ± SD	**2.38 ± 0.52**	**1.25 ± 1.19**	**99.14 ± 0.87**
Citro-bar Soap	V1	2.00	1.50	98.75
	V2	2.00	1.25	98.96
	V3	2.00	1.25	98.96
	V4	1.25	1.25	98.33
	Mean ± SD	**1.81 ± 0.38**	**1.31 ± 0.13**	**98.75 ± 0.30**
Life Trek, Mosquito Spray	V1	1.50	2.00	97.78
	V2	4.75	1.25	99.56
	V3	2.75	1.00	99.39
	V4	1.75	1.25	98.81
	Mean ± SD	**2.69 ± 1.48**	**1.38 ± 0.43**	**98.89 ± 0.80**
Medi Scabiol Soap	V1	3.75	0.50	99.78
	V2	3.25	1.00	99.49
	V3	2.25	0.75	99.44
	V4	3.25	1.75	99.10
	Mean ± SD	**3.13 ± 0.63**	**1.00 ± 0.54**	**99.45 ± 0.28**
Mosquito guard	V1	2.00	3.50	97.08
	V2	3.50	0.25	99.88
	V3	2.50	2.25	98.50
	V4	1.00	0.00	100.00
	Mean ± SD	**2.25 ± 1.04**	**1.50 ± 1.67**	**98.87 ± 1.37**
Anti-mozzie camping, outdoor and indoor cream	V1	4.75	1.50	99.47
	V2	7.00	3.25	99.23
	V3	5.00	1.75	99.42
	V4	4.00	1.25	99.48
	Mean ± SD	**5.19 ± 1.28**	**1.94 ± 0.90**	**99.40 ± 0.12**
No-squito lotion	V1	2.50	4.50	97.00
	V2	4.00	5.50	97.71
	V3	1.50	2.50	97.22
	V4	1.50	1.75	98.06
	Mean ± SD	**2.38 ± 1.18**	**3.56 ± 1.74**	**97.50 ± 0.48**

Pure Beginning	V1	8.75	2.25	99.57
Organic Care,	V2	7.50	2.75	99.39
100% Natural	V3	6.25	4.50	98.80
Insect	V4	4.25	1.00	99.61
Repellents	**Mean ± SD**	**6.69 ± 1.92**	**2.6 3± 1.45**	**99.34 ± 0.37**
Medic Insect	V1	7.75	4.00	99.14
Repellent	V2	5.00	3.50	98.83
Cream	V3	3.50	1.75	99.17
	V4	7.50	3.00	99.33
	Mean ± SD	**5.94 ± 2.05**	**3.06 ± 0.97**	**99.12 ± 0.21**
All-natural guard	V1	1.00	2.50	95.83
insect repellent	V2	2.00	1.50	98.75
	V3	5.25	0.75	99.76
	V4	1.00	0.50	99.17
	Mean ± SD	**1.56 ± 0.67**	**1.31 ± 0.90**	**98.38 ± 1.75**
So Pure	V1	2.00	4.00	96.67
Naturally,	V2	2.50	3.50	97.67
Mosquito Spray	V3	2.00	2.75	97.71
	V4	3.75	4.25	98.11
	Mean ± SD	**2.56 ± 0.83**	**3.63 ± 0.66**	**97.54 ± 0.61**
Moz-Free	V1	5.50	2.00	99.39
Mosquito	V2	7.00	1.00	99.76
Repellent	V3	2.00	0.50	99.58
	V4	3.50	5.00	97.62
	Mean ± SD	**4.50 ± 2.20**	**2.13 ± 2.02**	**99.09 ± 0.99**
Mylol perfumed	V1	2.50	0.75	99.50
mosquito	V2	4.00	2.00	99.17
repellent	V3	5.00	3.00	99.00
	V4	2.75	0.50	99.70
	Mean ± SD	**3.56 ± 1.16**	**1.56 ± 1.16**	**99.34 ± 0.32**
Mosquito Patch	V1	1.75	2.75	97.38
Insect	V2	0.50	0.00	100.00
Repellents	V3	3.00	1.75	99.03
	V4	0.50	1.50	95.00
	Mean ± SD	**1.44 ± 1.20**	**1.50 ± 1.14**	**97.85 ± 2.19**
Bennets, Mozzie	V1	5.50	0.75	99.77
stick	V2	2.50	1.50	99.00
	V3	3.25	3.00	98.46
	V4	4.75	3.00	98.95
	Mean ± SD	**4.00 ± 1.37**	**2.06 ± 1.13**	**99.05 ± 0.54**

The minimum mean percentage protections were obtained from the plant-based No-squito lotion with 97.50 ± 0.48% (Figure 3.41; Table 3.19).

The ANOVA analysis was performed on a transformed percentage data to compare the mean repellency between the control DEET based repellent (Tabard) and the other tested repellent products. There was a statistically significant difference in the mean repellency between two or more repellents tested (p=0.019). A *post hoc* test for multiple comparisons using the Turkey's honestly significant difference test (Turkey HSD), showed that there were no statistically significant differences between the mean of repellency of Tabard DEET-based insect repellents and the other fourteen repellent product tested (Figure 3.41)**.** However, statistically significant difference was only found between the mean repellency of Pure Beginning and Medic insect repellent cream (p=0.035).

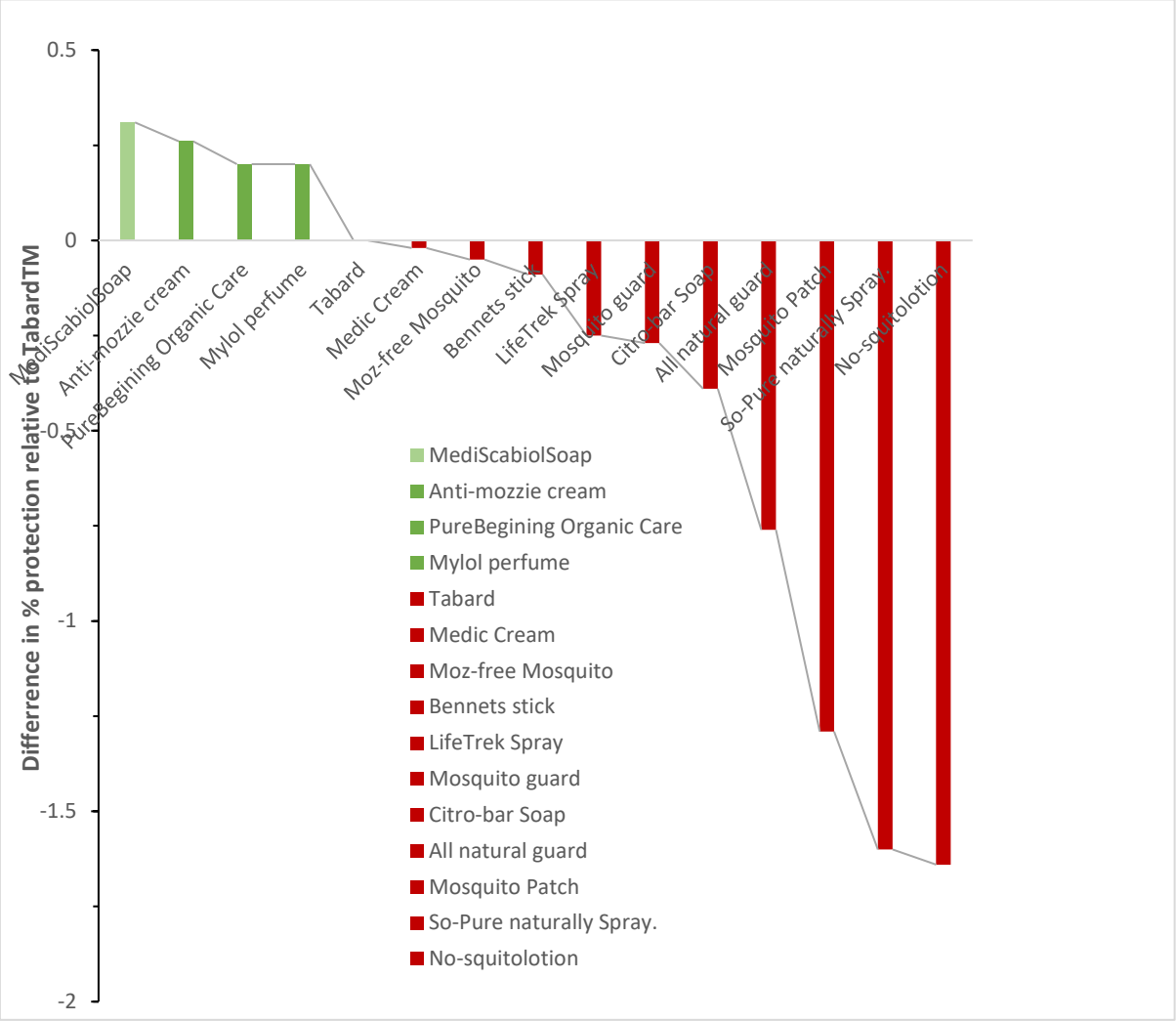


Figure 3.41: Shows differences of percentage protections of the tested repellents products relative to Tabard.

3.6.4 Spatial activity index and percentage responding

The spatial repellence of an active ingredient can be expressed in a form of a spatial activity index (SAI), which is defined as the proportion of mosquitoes prevented from entering the treatment chamber in relation to the total number of the mosquitoes moving within the system, as calculated by using Equation 2.2 (WHO, 2013). The SAI of all the fifteen repellents products tested ranged from -1 to 1. In this study, the calculated SAI ranges from 0.25 ± 0.10 as seen with All-Natural Guard insect repellent to -0.13 ± 0.18 seen with Medic Insect Repellent. Among the repellent products that were tested, nine had a positive SAI, five products including Tabard^{TM} had negative SAI, while one product So pure naturally did not show any spatial activity, with SAI of 0.00 ± 0.15 (Table 3.20 and Figure 3.41).

Table 3.20: Percentage responding, and Spatial activity index of the repellent products tested.

Where % Responding was calculated: $\frac{\mathbf{NCAC+NTAC}}{\mathbf{N}}$ ***and SAI calculated -*** $\left[\frac{NCAC-NTAC}{NCAC+NTAC}\right] \times \left(\frac{TNCT}{N}\right)$

Products	Replicate	NCAC	NTAC	%Responding	SAI
Tabard					
	V1	4.25	10.00	0.71	-0.29
	V2	6.25	2.00	0.41	0.21
	V3	6.00	8.25	0.71	-0.11
	V4	8.50	7.00	0.78	0.08
Mean SAI ± standard error					**-0.03 ± 0.11**
Citro-bar Soap					
	V1	10.75	4.25	0.75	0.33
	V2	6.50	9.00	0.78	-0.13
	V3	8.50	4.25	0.64	0.21
	V4	6.50	9.25	0.79	-0.14
Mean SAI ± standard error					**0.07 ± 0.12**

Life Trek, Mosquito Spray	V1	12.00	3.25	0.76	0.44
	V2	7.00	6.25	0.66	0.04
	V3	8.50	6.75	0.76	0.09
	V4	11.00	4.00	0.75	0.35
Mean SAI ± standard error					0.23 ± 0.10
Medi Scabiol Soap	V1	5.25	8.00	0.66	-0.14
	V2	7.75	6.75	0.73	0.05
	V3	6.75	8.50	0.76	-0.09
	V4	7.50	7.25	0.74	0.01
Mean SAI ± standard error					-0.04 ± 0.04
Mosquito guard	V1	7.25	4.25	0.58	0.15
	V2	8.25	4.25	0.63	0.20
	V3	7.00	5.50	0.63	0.08
	V4	9.25	5.75	0.75	0.18
Mean SAI ± standard error					0.15 ± 0.03
Anti-mozzie camping, outdoor and indoor cream	V1	-	-	-	-
	V2	-	-	-	-
	V3	-	-	-	-
	V4	6.50	4.00	0.53	0.13
Mean SAI ± standard error					0.13
No-squito lotion	V1	6.25	5.00	0.56	0.06
	V2	1.75	7.75	0.48	-0.30
	V3	8.25	7.50	0.79	0.04
	V4	5.75	7.50	0.66	-0.09
Mean SAI ± standard error					-0.07 ± 0.08
Pure Beginning.	V1	6.25	2.00	0.41	0.21
	V2	5.00	0.50	0.28	0.23
	V3	3.00	4.25	0.36	-0.06
	V4	9.00	5.25	0.71	0.19
Mean SAI ± standard error					0.14 ± 0.08
Medic Insect Repellent	V1	2.0	4.25	0.31	-0.11
	V2	1.25	7.75	0.45	-0.33
	V3	3.00	11.75	0.74	-0.44
	V4	10.75	3.25	0.70	0.38
Mean SAI ± standard error					-0.13 ± 0.18
All-natural guard	V1	12.50	3.50	0.80	0.45
	V2	9.75	3.25	0.65	0.33

	V3	9.25	4.75	0.70	0.23
	V4	9.00	9.25	0.91	-0.01
Mean SAI ± standard error					0.25 ± 0.10
So-Pure Naturally	V1	5.50	6.25	0.59	-0.04
	V2	6.50	6.50	0.65	0.00
	V3	6.25	8.50	0.74	-0.11
	V4	6.50	3.50	0.50	0.15
Mean SAI ± standard error					0.00 ± 0.15
Moz-free					
	V1	8.50	0.00	0.43	0.43
	V2	5.00	6.00	0.55	-0.05
	V3	6.50	11.00	0.88	-0.23
	V4	4.50	7.00	0.58	-0.13
Mean SAI ± standard error					0.01 ± 0.15
Mylol perfumed	V1	10.00	6.75	0.84	0.16
	V2	9.75	2.00	0.59	0.39
	V3	4.75	7.00	0.59	-0.11
	V4	11.50	4.75	0.81	0.34
Mean SAI ± standard error					0.20 ± 0.11
Mosquito Patch	V1	7.75	6.50	0.71	0.06
	V2	11.00	8.00	0.95	0.15
	V3	8.00	4.00	0.60	0.20
	V4	4.50	13.00	0.88	-0.43
Mean SAI ± standard error					-0.01 ± 0.14
Bennets, Mozzie stick	V1	4.75	3.25	0.40	0.08
	V2	7.00	7.75	0.74	-0.04
	V3	6.75	6.00	0.64	0.04
	V4	6.50	5.00	0.58	0.08
Mean SAI ± standard error					0.04 ± 0.03

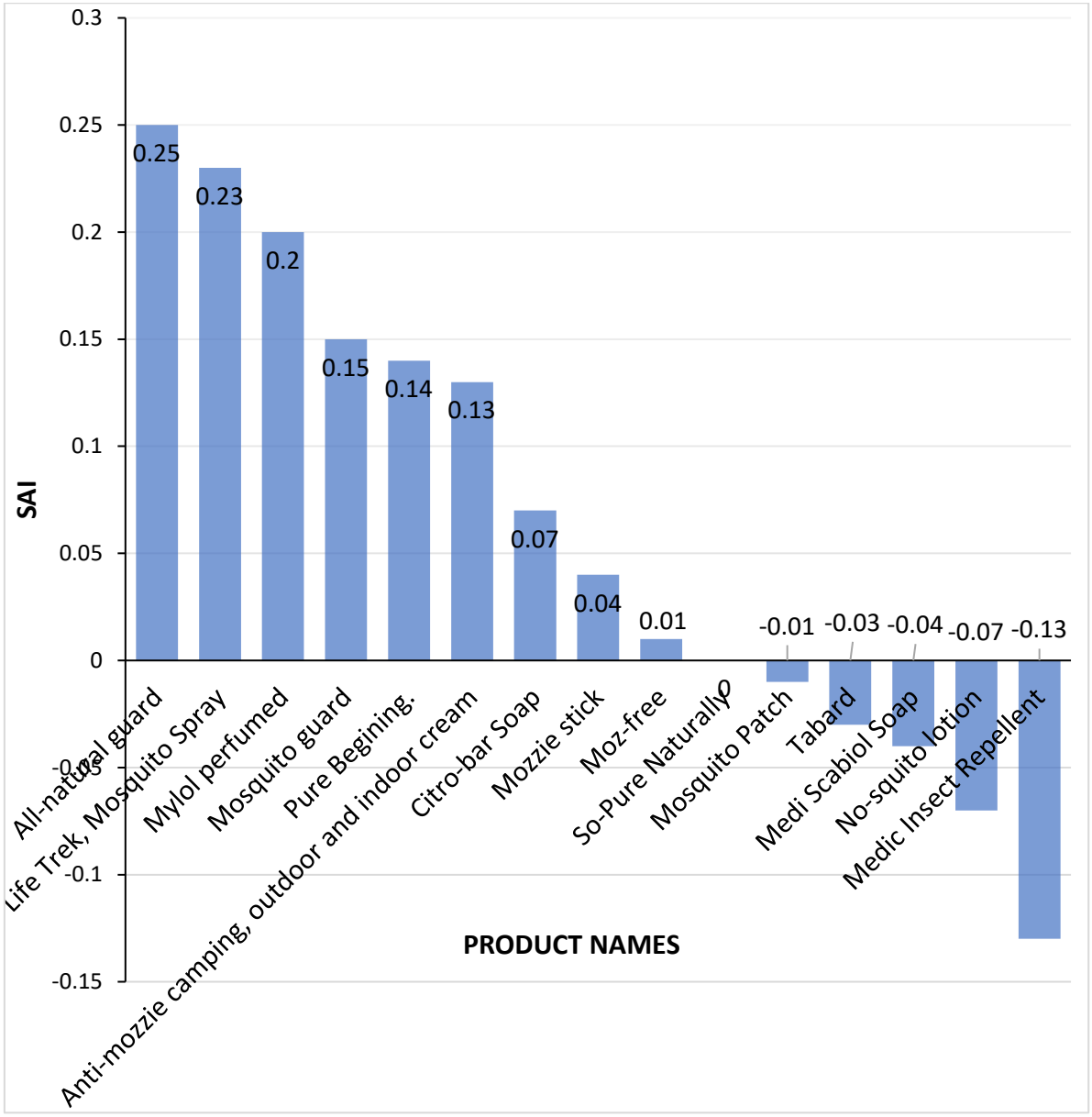


Figure 3.42: Bar chart showing the SAI of the tested repellent products.

CHAPTER FOUR:

CONCLUDING DISCUSSION

4.1 Introduction

This chapter aims to discuss the key findings presented during the data analysis in Chapter three in a clear and simple format, in relation to the research aims and objectives. Assessment and understanding of perceptions, attitudes, and practices of any community against malaria disease are very important in refining the development of malaria strategic policies towards malaria control and elimination (DePina et al., 2019). The community development and practices of the populations can guide and facilitate the implementation of an effective surveillance system that will help to achieve an elimination goal and to prevent resurgence (Liu et al., 2013).

This study aimed to assess and compare the malaria-related knowledge and preventive measures in South Africa and Nigeria and to assess the in vitro efficacy of the reported mosquitoes' repellents being used by the public in Johannesburg, South Africa. To the best of my knowledge, this is the first study that compared the malaria related knowledge and prevention practices between Nigeria and South Africa. It is also the first study that document the list of the commercially available mosquito repellents in Johannesburg, South Africa through market and online survey.

The findings of this study indicate a significant difference between the respondents living in a malaria endemic area in Birnin Kebbi metropolis, Nigeria compared to and the malaria-free Johannesburg, South Africa. Specifically in terms of their knowledge of malaria symptoms and transmission, mosquito breeding sites, understanding of an effective personal protective measure, treatment seeking behaviors and compliance to antimalarial medications.

4.2 Socio-Demographic Characteristics

Overall, most of the participants in this study were females (57.4%) with mostly South African females (62.1%) completing the questionnaire; whilst the converse occurred in Nigeria (Table 3.1). This trend has been reported before where in a large number of the African studies, female respondents predominantly took the time to complete a questionnaire (DePina et al., 2019; Manana et al., 2018). The reason for the slightly

higher number of males completing the form could be due to the higher male to female ratio of students attending Nigerian medical schools. In previous studies, a similar observation was made, where 55.8%, 58.9% and 61.3% male respondents were respectively reported to in the Northern part of Nigeria (Adiel et al., 2021), North central Nigeria (Oguntade et al., 2018) and Osun state, Nigeria (Edet-Utan et al., 2016).

The gender of the study participants differs significantly between the two countries ($p<0.001$) (Table 3.1). The 'other genders' were all reported from South Africa, and this is most likely be because of the Lesbian, gay, bisexual, transgender and intersex (LGBTI) Rights Law as stated in Section 9 of the South African constitution. This mandates that neither the state nor any non-state actor may: "unfairly discriminate directly or indirectly against anyone on one or more grounds, including race, gender, sex, pregnancy, marital status, ethnic or social origin, colour, sexual orientation, age, disability, religion, conscience, belief, culture, language and birth" (ConstitutionofSouthAfrica, 1996). Whilst in Nigeria the LGBTI are all criminalised and anybody found guilty can be either sentenced to death by stoning or 14 years imprisonment (GUARDIAN, 2014; HumanDignityTrust, 2022).

The educational status of the respondents also differs significantly between the two countries ($p<0.001$), where the majority of the respondents from both countries have a tertiary level of education. However, of the participants that did not attend school were for the majority from Nigeria (60%). These differences may be related to the difference in literacy levels between the two countries, namely, 62.02% in Nigeria, with over 10.5 million 5-14years out of school children compared to 87.0% literacy level in South Africa (Maverick Citizen, 2021; FAWCO, 2021).

Most of the study participants were within the age range of 21-40yrs (71.1%) (Figure 3.1). There were relatively younger participants from South Africa (mean: 24.78 ± 7.47 years) compared to those from Nigeria ($p<0.001$). This difference may be due to the fact that in Nigeria there are many over-aged students, with many repeat students. In addition, on average it would take Nigerian scholars nine years to complete their six-year primary school education (FAWCO, 2021).

The advent of COVID-19 pandemic and the lockdowns implemented by the South African government, adversely affected the data collection. The additional case load for the South African HCPs also adversely affected the number of responses received. As such there was a slightly higher proportion the HCP from Nigeria (52.1%); where

the majority were from Federal Medical Centre which is larger compared to the Sir Yahaya Memorial Hospital. In South Africa, the majority were from CMJAH. This could be due to the fact that the CMJAH is adjoined to the WITS Faculty of Health Sciences and allowed for easy access (TIPS, 2002a).

4.3 Participants Malaria-related Knowledge

4.3.1 Malaria transmission vector

Almost all the respondents from both countries have a very high level of understanding of the malaria transmission vector, with more than 91.8% of all respondents correctly associating a malaria infection with the bite of female *Anopheles* mosquito (Figure 3.8). This level of knowledge is comparable to that reported from Eritrea (91.8%) (Andegiorgish et al., 2019), 89.5% in Nigeria (Olayemi et al., 2012) and 92.1% from Mpumalanga, South Africa (Govere et al., 2000a). Although not as high as that reported in other studies from Mamfene, Kwazulu-Natal, South Africa (99%; Manana et al., 2018), India (97.0%; Kadam et al., 2015) and Ethiopia (95.6%; Abate et al., 2013). This decreased level of knowledge could be due to the fact that in Johannesburg malaria is not endemic and is only encountered when travelling to those malaria areas in South Africa (KwaZulu-Natal, Limpopo, Mpumalanga) or to neighbouring countries (SADOH, 2018). In contrast, the level of education appears to be more than that received in other countries where there was a lower level of knowledge on *Anopheles* as the malaria vector. This was reported for countries including, Ethiopia (86.2%; Teklemariam, 2018), Tanzania (63.2%; Sumari et al., 2016), Nigeria (77.5%; Udonwa et al., 2010) or Thailand (80.0%; Van Benthem et al., 2006).

With the higher occurrence of malaria in Nigeria, it was not unexpected that 97.10% of the Nigerian respondents were able to link malaria with the bite of a female *Anopheles* mosquitoes compared to those in South Africa (89.10%) ($p<0.001$). Almost all the HCPs (99.0%) correctly linked malaria with the *Anopheles* mosquito, with a slightly lower association by students (Nigeria, 96.5%; South Africa, 96.2%) and the public ($p<0.001$). However, despite this good correlation between vector and disease, there was surprisingly a small percentage of participants (1.3%) that associated malaria with eating contaminated food. With the majority (93.3%) of these respondents being South African students (Figure 3.9), who also identified swimming in river and ponds as the causative route of infection (0.7%). In addition, 2.4% of South Africans associated the cause of malaria with climatic changes compared to 1.6% from Nigeria (Figure 3.9).

None of the Nigerian students had similar misconceptions, however previous studies have noted that Nigerians have also reported these three misconceptions (Aju-Ameh et al., 2016; Olayemi et al., 2012).

These observed differences in responses could be related to the fact that malaria transmission is holoendemic all over Nigeria (FMOH, 2014); whilst in Johannesburg, South Africa it is sporadic and with mostly imported cases (SADOH, 2019a; Fox, Karstaedt, Menezes, 2021). This difference is in keeping with the findings of Van Benthem et al. (2006), who compared the malaria-related knowledge between those living in malaria endemic or non-endemic areas in Thailand. Similarly, these misconceptions have been reported in Eritrea (Andegiorgish et al., 2019) and Nambia (InfoNamiba, 2020).

Possible reasons for the Nigeria cohort being more informed on the malaria-*Anopheles* association, is that almost all the participants from Nigeria have had malaria in the past (Figure 3.20) and hence more aware of the association. In addition, it may be related to the varied level and frequency of health educations malaria programs that are delivered in the two study countries, with the likelihood that there are more malaria-related programs broadcast in Nigerian media stations compared to South Africa. As seen in this study, more Nigerians (34.0%) mentioned they obtained their information on malaria through radio and television compared to only 18.5% from South Africa (Table 3.7). Furthermore, mass media exposure has shown to play a pivotal role in improving malaria-related knowledge and adoption of healthy lifestyle (Yaya et al., 2018). These observations underscore the need for a public health intervention program to be tailored towards these observed misconceptions for a better and sustainable vector control programs in the study countries.

4.3.2 Mosquito breeding site

The availability of mosquito breeding sites is always a concern when trying to control malaria transmission and number of cases of malaria. With the higher occurrence of malaria in Nigeria, the association of malaria with *Anopheles* mosquitoes coincided with excellent knowledge that standing water was one of the main breeding sites for female *Anopheles* to lay her eggs and allow for their maturation (85.3%; Figure 3.12). The Nigerian participants, student and the public demonstrated a higher level of understanding compared to their South Africa counterparts. On the other hand, the

HCPs from South Africa had a higher level of knowledge compared to their colleagues from Nigeria (Section 3.2.1). The acknowledgement by all participants that standing water should be prevented is a favourable observation to note, as it translates in the fact the majority of people are contributing towards the reduction of mosquito numbers and malaria transmission in their immediate surroundings.

However, the differences observed between the HCPs of the two countries, may be relate to the extra implementation of training sessions by the South African government on vector control measures, which ensures that the South African HCPs are more aware of the causative vector and favourable breeding sites (WHO, 2015c).

One misconception that was identified in this study was that more respondents from South Africa believed that soil was a mosquito breeding site, whilst Nigerians believed that garbage was another potential breeding site. The latter observation was noted in several other site studies (Kulkarni et al., 2017; Mehta et al., 2015; Amaechi et al., 2018). The perception that garbage is a breeding site may be related to the differing refuse disposal systems in the two countries, where in Birnin Kebbi, Nigeria garbage is dumped on the street and in conjunction with the increased rain fall in Nigeria, it seems logical for Nigerian participants to consider garbage as a common breeding site. Under these circumstances if the garbage is not cleared or left undisturbed, it could be a favourable site for breeding. This observation has been noted in similar studies undertaken by Mehta et al. (2015) in an urban area of Bhavnagar, India. In contrast, the Johannesburg metropolitan has an advanced way of waste management (Pikitup, 2018),which reduced garbage in which water can accumulate.

The existence of these misconceptions on malaria breeding sites and transmission indicates again a need to improve and intensify education in all sectors of Nigeran and South Africa on malaria transmission-related health education.

4.3.3 Malaria transmission season

Nigeria has an annual rainfall of 600-1000mm and 1,300-1,800mm in the northern and southern parts of the country, respectively, with the rainfall reaching the highest between June and September in the north and between March to November in the south. These periods coincide with a peak in the number of malaria cases seen in the country each year (FMOH, 2014). In contrast, in South Africa the period in which the highest malaria transmission occurs is in the rainy season that spans between

September to May (SADOH, 2018a; Burke et al., 2019b). Most of the participants related the rainy season as the period with highest malaria transmission (Figure 3.14).

However, despite demonstrating excellent knowledge and awareness of the malaria transmission seasons in their respective countries, there were some misconceptions noted. A slightly higher proportions of the participants from South Africa mentioned the dry season as a period with the highest transmission compared to the Nigerian participants. However, the Nigerian participants mentioned that there was no difference in malaria transmission between these two seasons compared to the South Africans. The misconceptions about the malaria seasons may relate to the fact that with the holoendemic nature of malaria transmission in Nigeria, any decrease in mosquitoes or malaria cases during the dry season may not be significantly different to be observed by many citizens in Nigeria. This misconception was also observed by Andegiorgish et al. (2019) in Eritrea and in Namibia by Jacob and Nuuyoma (2019) and Ajao et al. (2017) among the university community in Nigeria**.**

4.3.4 Malaria-related symptoms

To successfully treat a *Plasmodium* malaria infection, diagnosis is an urgent, key skill that HCPs and those living in endemic areas need to be aware of. Classically, malaria presents with non-specific clinical features that may be confused with many pathologies, including influenza (SADOH, 2018). As such, a high index of suspicion is the most important element in the diagnosis of malaria. Malaria should be suspected in any person presenting with any of the symptoms such as fever, headache, body pains and rigors (Table 1.5; van Zyl, 2016).

Of these, the four most mentioned symptoms and signs identified by the respondents in this study were fever, chills, headache and nausea and vomiting (Figure 3.3). This finding was similar to that recorded by Manana et al. (2017) in Mamfene, Kwazulu-Natal, South Africa and in Nigeria by Okwa et al. (2011). When differentiating between the responses from the two groups in this study, it was observed that the South African HCPs and students were more familiar with these clinical symptoms (Figure 3.7 and 3.8). This difference may be related to the more rigorous education received in South Africa compared to Nigeria. The education system in South Africa was ranked 3rd in Africa based on labour competences, quality of schooling, digital literacy, capacity to think critically, and creatively and interpersonal skills, while Nigeria was not among the top ten African nations with finest education (BSCHOLARLY, 2022). In contrast to the responses of the HCPs and students, the public respondents in Nigeria had more

practical experience when encountering malaria and able to recognise the symptoms more effectively than those in South Africa (Figures 3.5 and 3.6), where malaria elimination is just a matter of time (FMOH, 2014; Maharaj et al., 2019). A similar observation was made in Thailand (Van Benthem et al., 2006) and India (Manohar et al., 2017) where large differences were observed in malaria knowledge between people living in malaria endemic and malaria-free areas.

A disappointing outcome of the study was that only 46.2% of the respondents were able to identify all four of the most mentioned symptoms, which was quite below (63.0%) reported by Manana et al. (2017) in Mamfene, Kwazulu-Natal. The observed differences may be due to the participants in Mamfene were living in a malaria transmission area and were expected to be more familiar with the malaria-related symptoms and signs, than the Johannesburg participants living in a malaria-free area. Furthermore, only 33.8% of the participants associated all seven symptoms presented to them with malaria, namely fever, chills, headache, nausea and vomiting, joint pains, abdominal pain and convulsions. This outcome was comparable to the 38.0% obtained by Van Benthem et al. (2006) in Thailand. More participants from South Africa (35.6%) associated all the seven symptoms with malaria compared to those from Nigeria (30.4%) and this may be associated to the higher literacy level and education standard in South Africa, since students were included in this study (BSCHOLARLY, 2022). In contrast, a significantly higher proportion of the HCPs (47.0%; $p<0.001$) correctly identified all the seven symptoms compared to the students and public. A comparable finding was reported by Onwujekwe et al. (2009) the hospitals staff were compared to non-hospital participants in the southeastern part of Nigeria.

4.3.5 Malaria control strategies

Malaria control strategies including LLINS, IRS, ACT, strengthening of healthcare systems, insecticide spraying programmes and use of intermittent preventive therapy in pregnancy (Section 1.4) are proven methods to reduce the incidence of malaria and vector control. Overall, the participants had a poor concept of malaria control strategies with less than half of the participants knew IRS, health promotion and case management formed part of the malaria control strategies (Table 3.4). Of the strategies used, LLINs was known by the majority of the study participants (72.3%); with the Nigerian public respondents displaying the highest level of knowledge on LLINs use compared to the other groups (Table 3.5). The significant difference between the two study countries is possibly due to the necessity for those living in Nigeria to know and

implement the use of LLINs. Several reports by Beyene et al. (2015) in Ethiopia, Manana et al. (2018) in South Africa and Dawaki et al. (2016) in northwestern part of Nigeria, all indicated that LLINS is the most commonly known strategy against malaria infections. .

4.3.6 Sources of information on malaria and request for further malaria education

Educating the community and reinforcing this knowledge in HCPs is of utmost importance. In this study, the major source of information (55.5%) was reported to be at the school level (tertiary), but this finding could have been skewed as the students constituted more 55.2% of the study population. The participants from South Africa were twice as likely to obtain the information on malaria from schools than those in Nigeria ($p<0.001$)

The hospitals served as a source of information to only 33.4% of the all the study participants, with only 28.4% by South African hospitals sharing information on malaria. This was comparable to 20.7% as reported by Uma et al. (2016) from a malaria non-endemic area in India However, the hospitals served as the highest source of information on malaria for the participants from Nigeria (46.8%), which was comparable to 44.7% obtained by Uma et al. (2016) in a malaria endemic area of India; but approximately half that reported by Ghanaians (Laar et al., 2013). These findings indicate the need to intensify more effort for awareness creation on malaria by the HCPs in both countries.

Resources accessible to South Africans for malaria-related information was twice as likely to be from newspapers and friends compared to Nigerians population, who mostly (34.0%) obtained their malaria-related information from radio and television compared to 18.5% from South Africa (Table 3.5). This could have been due to the literacy difference between the two countries to deliver a verbal form of information sharing or the need for Nigeria to be able to reach more or the population to alert the population of threats of malaria and how to control transmission. Also, the participants in South Africa are more likely to discuss malaria with their colleagues, because they perceived it as a serious disease compared to Nigerians who think malaria forms part of their everyday life (FAWCO, 2021; Maverick Citizen, 2021).

Unfortunately, more than half of the participants (51.9%) indicated that they do not have enough information on malaria and requested for further malaria-related health

education; to focus predominantly on malaria treatment. The South Africans indicated that they were more likely to request more information related to treatment, prevention and nature of the disease compared to malaria control by the Nigerian participants (Table 3.7). This difference in information seeking behaviour could be related to the participants' attitudes toward malaria, where most of the Nigerian participants and those living in endemic areas (such as in Colombia) may not consider malaria to be a serious disease with most believing that being infected with malaria is a normal part of life (Forero et al., 2014). In contrast, the South African participants considered malaria as a serious disease, as such wanted to know much more about the nature of the disease, prevention and treatment of malaria.

4.3.7 Anaemia and family history of blood transfusion due to malaria

Anaemia is a common complication of malaria, although it has many causes. As such, it is important that both HCPs and the public are aware that anaemia is linked to malaria infections and should be monitored. Overall, the respondent's knowledge on anaemia as a complication of malaria was good (79.8%), being significantly higher among the Nigerian respondents than those from South Africa. This would positively contribute to the higher index of suspicion of anaemia among the Nigerian HCPs, which will led to the successful treatment of the patient; hence the Nigerian HCPs are more likely to diagnose malaria-related anaemia than the South African HCPs. To rectify anaemia and adjust the haematocrit, a blood transfusion may be required (SADOH, 2019). Of the study participants, only 14.6% had a family history of blood transfusion, with 33.7% and 5.0% of the Nigerian and South African participants, respectively, reporting a history of blood transfusion ($p<0.001$; Figure 3.12). The majority of those receiving the transfusion were within the public respondents and tentatively linked to their low socio-economic status (Barat et al., 2004; Nwaneri and Sadoh, 2020; Nkegbe et al., 2017). These observed differences could be related to the differences in the intensity of malaria transmission between Nigeria and South Africa. In fact, it has been documented that malaria-related anaemia is more common in countries with intense malaria transmission with the highest moderate/severe anaemia prevalence was found in Burkina Faso (69.6%), Guinea, Ghana, Cameroon, as well as Nigeria (Olanrewaju and Johnson, 2001; Papaioannou, Utzinger and Vounatsou, 2019).

4.3.8 Overall malaria knowledge score

Based on the key aspects of malaria Overall, 68.8% of the study participants have good knowledge on malaria, where the South Africans (73.8%) had a significantly

higher score than their Nigerian (59.2%) counterparts (p <0.001). This finding was comparable to 74.3% reported by Fuge et al. 2015) for an Ethiopian cohort and 50.4% in Southern Ethiopia (Kebede et al., 2017). Again, education appears to be a key factor in ensuring that HCPs and medical students can optimally manage their patients. Although living in an endemic environment constantly exposes the public to the risk of being infected, there should not be complacency on behalf of the public, HCPs, and government to jeopardise the health of the community. Education of the women in the household tends to lend itself for the continued teaching within the home and the increased awareness of malaria-related aspects was shown in this study (Figure 3.22). However, continued exposure to the dangers of malaria through all media platforms should continue to ensure the wider community regardless of education level, is reached and empowered to confidently defend against a malaria infection.

This study indicated that most of the study participants had good knowledge on various aspects of malaria, with the HCPs and students from South Africa displaying better knowledge than their Nigerian counterpart. In contrast, the Nigerian public respondents revealed they were more informed on the various aspects of malaria compared to the South African public respondents. Although high scores were obtained for the majority of the aspects investigated, there is room for improvement with additional and continued education to reinforce habits and behaviours to decrease the risk of a malaria infection and to optimise the management of the infected person.

4.4 Participants Attitudes and Perceptions on Malaria Prevention and Management

Attitudes is simply an individual subjective and personal opinion about a specific topic. While perceptions are expression of one's attitude and it is simply an individual belief or opinion based on how he or she understood and interpreted the subject of discussion (KeaneCreative, 1997; Beri, 2009).

In general, the majority of the participants (93.6%) knew that malaria can be prevented with early treatment, where there was a slightly higher proportion of participants from South Africa (93.7%) that believed malaria can be prevented compared to 93.4% from Nigeria. This difference may be due to the fact that South Africa is almost at the verge of malaria eradication throughout the country and the respondents had seen a practical aspect of a successful eradication programme along with medication that effectively treats patients. In contrast, Nigeria is still battling with a very high burden of malaria,

being the highest contributor to the world malaria burden (WHO, 2021; Raman et al., 2020). This high infective rate coupled with unsuccessful government programmes to manage vector breeding sites and patient management, would affect the attitude and perception of someone having to constantly be on guard against being infected (Akogun, 2008; FMOH, 2014; Forero et al., 2014)

Being on the forefront of malaria and other health-related issues, coupled with prevention or elimination programmes, the HCPs have seen the positive outcomes of early treatment. This was reflected in this survey, with HCPs responding that they knew malaria was a preventable disease compared to students and public respondents ($p<0.001$) (Section 3.3.1).

Even though Nigerian HCPs manage more malaria infected patients than their South African counterparts, the HCPs from South Africa indicated a slightly more positive attitude (97.9%) that malaria is a preventable disease compared to their counterparts from Nigeria (95.9%). This could have been reflective of the number of successful cases treated and fatalities observed by the Nigerian HCPs compared to the much lower number of cases managed by their South African colleagues. Whilst an almost equal attitude was noted amongst the students from both countries (Figures 3.22 and 3.23).

4.4.1 Treatment seeking behaviours

Symptoms and signs of *P. falciparum* malaria normally present within 10 to 21 days after being bitten by an infected vector mosquito but have been reported as early as 6 days. Recognition of clinical symptoms and a positive diagnostic test is recommended by the South African Department of Health before initiating treatment (SADOH, 2019). Slightly more than half (56.5%) of the study participants were in compliance with this recommendation, where they were willing to go for an early treatment within 24 hours of suspecting they were infected with malaria (Figure 3.18). This correlated to a higher proportion of South Africans (59.6%) indicating they would seek early treatment, compared to 50.8% from Nigeria ($p=0.001$). However, most of the participants that said they would wait until for seven days or more; such that this gave them time to try an over-the-counter medication for self-medication (Figure 3.19). This response was received from more of the Nigerian respondents (6.4%). This in itself could lead to complications and developing moderate to severe malaria. In South Africa, medication to treat malaria is not available over the counter only prophylactic medication. The fact

that this is not widely known, could further delay treatment whilst waiting for a medical appointment and the prescribed medication to be dispensed. A similar observation was reported by Anumudu et al. (2006) in a study conducted among Nigerian university students, where 25.0% of the respondents reported using self-medication once they suspected they were infected with malaria. The regular frequency in which Nigerians are infected makes it part of their life and is considered by many as not being a serious disease (Forero et al., 2014).

Surprisingly, eight participants, all from South Africa (Figure 3.19) said they would wait until the symptoms get serious before seeking treatment. This is a very dangerous attitude, as any delay in initiating malaria treatment especially in non-immune individual can lead to the severe form of the disease and increase the risk of mortality, where most South Africans were considered to be non-immune even those living in the malaria transmission provinces (SADOH, 2018). This indicated the need for an increased effort to provide malaria-related health education within the country. This is particularly true in South Africa and with such an attitude it could compromise the reduction or termination of malaria transmission in these areas. The infected individual could be harbouring many sexual forms of the *Plasmodium* parasite which could be transmitted to another person following a mosquito bite.

In this study, the participants' malaria treatment seeking behaviour was found to be statistically linked to the participants level of education across the two countries ($p=0.002$). Higher proportions of participants with tertiary level of education indicated that early treatment within 24 hours was preferred compared to those with a primary or secondary level of education or unschooled respondents (section 3.3.1). A similar finding was reported by Urama et al. (2021). In additon to education levels, other influencing factors could be finanacial where the latter respondants were unable to travel to the health clinic due to work or finance challenges. Whilst for university or HCPs, their locality near a clinic or campus health assisted with seeking treatment within the recommended 24 hours.

Previous studies have reported that the attitude of an individuals who had endured the experience of a malaria infection would seek malaria treatment earlier than before (Urama et al., 2021; Marsh et al., 2020). This was however not observed in this study, where Nigerians who had been previously infected indicated that they would delay seeking medical attention (Figure 3.18).

4.4.2 Attitude towards malaria preventive measures and treatment

The majority of the participants demonstrated a positive attitude with regards to malaria preventive measures, where LLINs (81.3%) and mosquito repellents (73.7%) were commonly mentioned. Nigerians favoured LLINs (82.9%) slightly more than South Africans livign in Johannesburg (80.5%)(p=0.684), as well as those living in the Limpopo province (82.0%). Antimalarial prophylactic medication was favoured by more than half of the respondents, along with having clean environment (Table 3.11), with the South African respondents preferring antimalarial drug prophylaxis more than Nigerians. These findings were corroborated by the observations in previously studies by Van Benthem et al. (2006), Teklemariam (2018) and Manana et al. (2018). Furthermore, more respondents from South Africa preferred the use of mosquito repellents (82.7%) for personal protection from a malaria infection, compared to 55.7% of Nigerians.

The South African Department of Health recommends for mild to moderate infections, the use of Coartem™ (artemether + lumefantrine) or if not available quinine + clindamycin/doxycycline (SADOH, 2019). These recommendations are relatively new where quinine + clindamycin/doxycycline was the preferred choice for mild to moderate infections and is still preferred for the treatment of women in the first trimester of pregnancy (SADOH, 2019). Surprisingly, a relatively low proportion of the respondents used Coartem™ (56.7%) and quinine (27.6%); where more respondents from Nigeria used Coartem™ (68.7%) compared to 33.5% in South Africa (P<0.001). Whilst quinine was used more in South African (61.7%) compared to Nigeria (9.9%)(Table 3.14). A large proportion of the HCPs in South Africa still believe that quinine is the preferred choice for the treatment of severe malaria (Figure 3.39). These differences in medication administration, may be related to firstly, that the South African HCPs were not up-to-date with the current guidelines to treat malaria, compared to their Nigerian counterparts. Secondly, the different demands of medications on the two Departments of Health based on the endemicity of malaria, drug sensitivity, drug availability and population profile in Nigeria (FMOH, 2014; Bamiselu et al., 2016).

To ensure complete clearance of the parasite from the blood stream, infected patients are counselled to complete the medication as prescribed. This study confirmed that the majority of the respondents (80.2%) completed their prescribed medications, with an equal proportion in South African and Nigeria. A similar finding was reported from Ghana (Afaya et al., 2017). However, a good number of the study participants indicated

that they do not usually complete their prescribed medications (19.8%) as they believe they have recovered i.e., asymptomatic. However, this does not mean they are parasite-free. Such behavior and poor attitude can lead to the development ore selection of resistant parasites, which can further compromise lives, the countries health system and countries economy (Ajonina et al., 2019; Afaya et al., 2017). These findings indicate that all citizens should be further educated on the dangers of the development of drug resistance, and the implication on successfully providing treatment of a previously curable infection. Also, the HCPs need to do more in educating their patients on the important of a drug adherence.

4.4.3 Overall malaria attitude score

It was unexpected to determine from this study that overall only 56.6% of the study participants demonstrated a good attitude towards malaria, with the South African (61.8%) participants showing a higher degree of knowledge towards key concepts and knowledge required to protect themselves from infection and treatment, compared to the Nigerian cohort (46.7%). However, this is in line with reports from Southern Ethiopia (55.1%) (Kebede et al., 2017) and 55.8% from Rwanda (Habimana et al., 2016). When considering factors which could affect this attitude score on malaria it was found that there was an association with participants gender, educational status, occupational status and age. A similar observation was made by Habimana et al. (2016) in Rwanda and (Oguntade et al.(2018) in North central Nigeria. But a concerning factor was the possible complacency of the Nigerian cohort as it is part of their daily lives and they believed that malaria is not a serious illness (FMOH, 2014; FAWCO, 2021). Of those included in the study, the more favourable attitudes of the HCPs indicate that this group of individuals should be more interactive with their communties to supplement and advance their knowledge as to the benefits of managing bredding sites to reduce the risk of infection and ensure all comply with treatment regimens to reduce malara transmission.

4.5 HCPs Knowledge on Management of Malaria

The study has shown that South Africans HCPs were more familiar with the RDT for malaria diagnosis compared to Nigerian HCPs who were more familiar with the microscopy (Figure 3.28). More Nigerian HCPs demonstrated good knowledge on the first line therapies for treatment of an uncomplicated and severe malaria compared to their South African counterpart (Figure 3.30 and 3.32). However, more South African

HCPs correctly prescribed the correct dosage of parenteral artesunate for the treatment of malaria compared to Nigerian HCPs (Figure 3.32 – 3.35).

4.5.1 Malaria diagnostic methods

In practice malaria diagnosis involves history taking, clinical examination, and definitive diagnosis with either RDT or microscopy before the commencement of chemotherapy. This is to avoid misdiagnosis which often result to an unnecessary exposure to the antimalarial medications due to misdiagnosis, severe illness, or death (SADOH, 2019). Malarias' clinical presentation is similar to many other diseases including influenza, viral hepatitis, encephalitis, septicaemia, meningitis, tick bite fever, gastroenteritis, typhoid fever, viral haemorrhagic fever, trypanosomiasis, HIV seroconversion illness, urinary tract infection and relapsing fever (SADOH, 2019).

Overall, microscopy was the most mentioned malaria diagnostic method (74.0%), followed by RDT (73.7%), which corresponds to studies done in Ghana (Prah et al., 2019) and in Zamfara State, Nigerian (Usman et al., 2018). The HCPs from South Africa were more familiar with RDT (78.8%) as a malaria diagnostic tool, compared to Nigerians HCPs who were more familiar with microscopy (72.0%) (Figure 3.28). These differences may be attributed to the perception by Nigerian HCPs that RDT are unreliable and that there is in fact a higher level of presumptive malaria diagnosis in malaria endemic areas (Bamiselu et al., 2016). Despite these differences, the HCPs from both countries had a relatively good knowledge of malaria diagnostic methods, which would support the WHO request for all cases of malaria to be tested with either RDT or microcopy or both to confirm the diagnosis. This also aligns with the WHO campaign to test, treat and track method in malaria management to improve the quality of malaria care and surveillance (WHO, 2015b).

Based on this latter finding, it indicates that the Nigerian HCPs have confidence in the skill of the microscopists in their respective laboratories. Since a diagnosis of malaria cannot be confirmed or excluded purely on the clinical symptoms, an accurate diagnosis relies on either microscopy or RDT as an essential tool for the successful management of a malaria case. The accuracy of the light microscopical method is dependent on well trained and skilful microscopists and good materials and equipment, who required regular training workshops to heighten their skills. Microscopists and laboratory technicians should be skilled in not only identifying a *Plasmodium* infection but should be skilful enough to differentiation between the species of *Plasmodium* to ensure the correct treatment regimen is administered (Luo eta al., 2021). Other factors

which could affect the reliability of the outcome of the RT strip and there by affect the HCPs opinion of the efficacy of this diagnostic tool, are the storage facilities required for the new RDT strips, as well as its transport to and from the clinic to the diagnostic laboratories, Ideally the strip should not be exposed to high temperatures and be stored optimally at the recommended temperature storage range of 1°C to 40°C, however WHO recommends 30°C depending of the manufacturer, and transported in a cool environment out of direct sunlight, but not frozen (WHO, 2009b). In addition, the RDT have been reported to not be able to reliably detect low-density parasitaemia (≤200 parasites/μL)(McMorrow, Aidoo, Kachur, 2011), where if there is a semi-immunity within the population in the endemic area, this will compromise eradication of the parasite and facilitate transmission.

4.5.2 Malaria chemotherapy

Globally, artemether plus lumefantrine and artesunate are the recommended therapies for the management of an uncomplicated and severe malaria, respectively (FMOH, 2014; WHO, 2015b; SADOH, 2019). Overall, 67.4% and 61.1% of the HCPs mentioned artemether plus lumefantrine and artesunate as the approved first line medications for the treatment of an uncomplicated and severe malaria respectively (Figures 3.31 and 3.32). The HCPs from Nigeria demonstrated a good knowledge of the first line therapies in accordance with their national guidelines, compared to South African HCPs (Figure 3.30 and 3.32). This difference may be attributed to the large number of cases HCPs manage in Nigeria, where about 60% of outpatient visits and 30% of hospitalizations in the country (FMOH, 2009).

South African HCPs identified ACTs (Coartem™; 54.9%) and artesunate (55.0%) as the first line therapies of an uncomplicated and severe malaria, which could be considered a reasonable score considering Johannesburg is a non-endemic area. However, there is a high number of travel malaria cases reported each year, which doctors in this area need to be able to optimally treat (Fox, Karstaedt, Menezes, 2021). The update to the guidelines on preventing and treating malaria was published in 2018 and 2019, respectively, and this may have affected the selection of quinine as the first line therapy which was the case for so many years (SADOH, 2018, 2019). However, despite the uncertainty as what to use as first line therapy, higher proportions of South African HCPs were able to correctly identify the correct dosage to use in various weight categories of patients. Where 12.6% of HCPs from South Africa correctly prescribed three doses of 2.4mg/kg of parenteral artesunate at 0, 12 and 24 hours for patient over

20kg (FMOH, 2014; SADOH, 2019), compared to only 9.8% of HCPs from Nigeria ($p<0.001$) (Figures 3.34 and 3.35). These findings were slightly better than those of Kalilani-Phiri et al. (2011) and Ahir and Bala, (2012) who reported a low percentage of correct prescriptions regimens of an artesunate (9.8%) for patient > 20kg and 6.3% for patient < 20kg.

A significant difference was noted between the two countries in selecting artesunate for the treatment of severe malaria, even though it is in line with the current recommendations worldwide (WHO, 2015b ; SADOH, 2019). Of the 62.3% HCPs who jointly preferred artesunate, 69.8% of Nigerian and 54.5% of South Africans made this choice. The fact that artesunate used to be only available on a patient named basis could have affected this selection, but this has altered where the Department of Health has made this drug more freely available. it was noted that there was a small percentage (12.1%) of HCPs who still believed and preferred quinine for the management of severe malaria (South African HCPs: 13.4% vs 10.8% from Nigeria). This could have been based on the clinical experience of the HCPs in using quinine knowing how to tailor the dose for their patient to avoid adverse effects (Table/section) (Umar et al., 2011).

But what is of concern is that 21.6% of the South African HCPs respondents did not know what the first line therapy of malaria treatment was (Figure 3.30 and 3.32). This could have been influenced by the profession of the HCP who completed the form, where medics, pharmacists, nurses could have been more aware with this information than physiotherapists and laboratory scientists. Although some doctors who have specialized in field which would not encounter malaria have also indicated that they were not knowledgeable on malaria guidelines (Kalilani-Phiri et al., 2011). This observation has been seen in other countries where Ghouth (2013) reported that one of the reasons why some clinicians continue to prescribe unrecommended or second line antimalarial agents was due to their poor knowledge on the new treatment policy or they had not ever read a clinical guideline or they believed the clinical guideline would not improve their diagnosis and treatment capability (Bhagat and Nyazema 2001; Ray and Nair , 2011).

These findings necessitate the implementation of regular educational workshops to update HCPs with the current guidelines to sensitize them to the current treatments

and abate misconceptions. This training should ideally be extended to include all the students training in healthcare and the public (Kamal-Yanni et al., 2012).

4.5.3 Knowledge of malaria chemoprophylaxis

Three options of malaria chemoprophylaxis are nationally approved and available in the African region viz: doxycycline, atovaquone–proguanil and mefloquine (SADOH, 2018; CDC, 2021). Atovaquone-proguanil was mentioned by 34.3% of the HCPs as the most known malaria chemoprophylaxis in this study (Table 3.15), with South African HCPs. This could be linked to the fact that there is a higher adherence to this drug compared to the two possible options. Landman et al. (2014) reported 88.0% adherence to atovaquone-proguanil compared to 82.0% for doxycycline and 62.0% for mefloquine. This preference for atovaquone-proguanil, especially in Nigeria (Table 3.15) could also be due to the fewer reported side effects to this medication; especially as it lacks neuropsychiatric side effects as mefloquine does (Meltzer and Schwartz, 2019; Dirk van der Berg et al., 1999). While the preference for doxycycline by South Africans (57.6%) is potentially a costing factor and awareness of the potential adverse effects since there is a likelihood that the drug had been taken before for another bacterial infection (Rodrigues et al., 2019).

WHO recommended that malaria chemoprophylaxis regimens include daily doses of doxycycline or atovaquone-proguanil to be started 1 to 2 days before arriving at malaria risk areas (Table 1.4). While a weekly dose of mefloquine was recommended to be started two to three weeks before departure, to monitor for potential unwanted side-effects and allowing time to alter medication to a more tolerated drug and to ensure the plasma level was optimal to protect against any *Plasmodium* parasites (WHO, 2012). This study indicated that the South African HCPs were able to provide the correct regimen for malaria chemoprophylaxis compared to their Nigeria colleagues (Figure 3.36).

Mefloquine has a set of contraindications that need to be considered before it can be prescribed, these contraindications include infant weighing less than five kilograms, history of epilepsy or psychiatric illness, underlying cardiac disturbances or arrhythmias, and past severe reactions to mefloquine (SADOH, 2017; CDC, 2021). This study has highlighted the fact that HCPs were not adequately aware of the contraindications as to when not to use mefloquine, where the better-known contraindications were previous history of an epilepsy and psychiatric illness (26.0%)

(Figure 3.37). The most reported contraindication to mefloquine use by both South African and Nigerian HCPs was a history of severe reaction to mefloquine. However, misconceptions that mefloquine should be avoided in pregnancy was higher among the South African HCPs (35.8%) compared to 17.7% for the Nigerian HCPs (Figure 3.36). Again, this is indicative that the South African HCPs have not updated their knowledge as the recommendations have been adjusted; where mefloquine has been approved by WHO for use from the first trimester of pregnancy. This was for both prophylaxis and treatment of malaria (SADOH, 2018; Labama Otuli et al., 2021). To note mefloquine is not registered to be used for treatment of malaria infected patients in South Africa, only for preventative therapy (SADOH, 2018).

Again, these findings necessitate the implementation of regular educational workshops to update HCPs with the current guidelines. The need for HCPs as well as the public to remain vigilant and to ensure they are aware of medication to prevent and treat malaria is still essential, whilst the two respective governments tackle the burden of malaria. In South Africa, there is a focus approach for malaria elimination within all its territories by year 2026, as well as assisting neighbouring countries where there is a higher burden than in South Africa. In contrast, Nigeria continues to battle with a higher burden of malaria within the whole country, needing to control vector breeding sites as well as ensuring the availability of skilled HCP and medication to manage of infected patients (FMOH, 2014; Njau et al., 2021).

4.5.4 Malaria-related information shared by the HCPs

This study has shown that the HCPs cohort of the study participants were better informed with regards to malaria prevention and treatment and as such should be at the forefront to educate the public and share their clinical expertise with students. A higher proportion of HCPs (72.9%) indicated that they always educate their malaria-positive patients with relevant information. Although this tended to be more by the Nigerian HCPs (81.9%) than the South African HCPs (62.8%) (figure 3.38). This may be due to the fact that the Nigerian HCPs are in contact with malaria-positive patient more regularly than their South African counterparts. The South African HCPs were more likely to counsel patients on preventative measures and backup treatment medication to those patients who were to be travelling to a malaria area. However, this statistic should be improved upon to better contribute towards the national programme to eliminate malaria and this can only be done if HCPs are part of the educational effort. HCPs reportedly did not make their patients aware of critical alerts. Namely, only

45.2% of doctors advised their uncomplicated malaria-positive patients to return to the hospital once they notice any complications, only 44.8% educated their patients on drug adherence and only 30.8% educated their patient on early treatment seeking behaviours (Table 3.38). Regretfully this appears to be a trend where little is gained by patients when interacting with HCPs (Yamamoto et al., 2010; Rowe et al., 2005; Ladi-Akinyemi et al., 2018).

Hence, the findings in this study gives an insight to the urgent need to deliver an organised malaria-related programs to update HCPs with the new policies to motivate them for malaria-related information sharing which would be an immense benefit in both countries.

4.6 Market and Online Surveys on Mosquito Repellents

One of the objectives of this study was to survey and document the repellent products that are available for purchase by the customers in Johannesburg, either physically in the shops or malls or by an online transaction. This appears to be the first time such information has been collated for the South African market.

In total, 92 different repellent products were identified with the majority obtained from an online search (77.2%). Out of these 46 were natural products, 10 synthetic repellents products, while 15 were based on electrical repellent mechanisms (Table 3.16 and 3.17). The cost of these repellents ranged from R12.49 to R1,252.57 with a median cost of R99.00; with the online products (R204.99 ± 235.97) significantly more costly than the market/store products (R51.64 ± 24.33) ($p<0.001$). This was similar to the costing of repellents performed in Thailand by Mulla et al. (2001), who reported that the cost of personal protective measures was between $12.50 and $25.00, i.e. R192.13 to R384.25 at R15.37 per dollar).

The South African government recommends that all products that are to be used or consumed by humans have to be approved by the South African National Accreditation System (SANAS), which is the only national body responsible for carrying out accreditations in respect of conformity assessment, as mandated through the Accreditation for Conformity Assessment, Calibration and Good Laboratory Practice Act (Act 19 of 2006) (SANAS, 2022). The SABS Certification Mark acts as a third-party guarantee of a product's quality, safety, and reliability, assuring consumers that the product conforms to specifications based on ISO / IEC 17065. Upon investigation into

the SAPB approval status of the collated products, it was found that overall only 55.2% of the surveyed products were approved in South Africa; whilst the information acquired on the product or on the website did not specify their SABS approval. However, not all of those products indicating approval could be traced in the South African health products regulatory authority's registered health products list (SAHPRA, 2022).

The citronella oil was the commonest ingredients (33.4%) contained in most of the surveyed repellent products, with the majority of the repellents being plant-based products. This may be related to the recent surge of research to find an ideal and ecofriendly natural repellent product (Rehman et al., 2014). The plant-based products are increasingly gaining popularity among consumers because they are believed to be safer than the synthetic products (Shukla et al., 2018).

The synthetic repellent, DEET only found in 7.3% of the surveyed products (Figure 3.40). It is regarded as the gold standard product, and it is recommended for a long-term protection (Xu et al., 2014).

Many varied electrically powered products were identified in this survey with the majority emitting either ultraviolet light or sound wave to repel mosquitoes (Table 3.16). The soundwave-based electric repellents use the natural behaviour of female mosquitoes in which they avoid male mosquitoes during her egg laying period. They do this by detecting the sound produced by the males and avoiding him. As such, these devices produces sound similar to that of male mosquitoes, thus repelling the female mosquitoes such that she does not bite a human host (Feng, 2001). However, most of the scientific studies that assess the efficacy of an electrically powered mosquito repellent devices concluded that these products do not provide any significant protections against mosquitoes, especially those that uses sound wave and wearable devices (Enayati et al., 2007; Rodriguez et al., 2017).

Prevention of a mosquito bite remains one of the most important mainstays of malaria prophylaxis. The application of a 20–50% diethyltoluamide (DEET) insect repellent to the exposed skin along with wearing permethrin impregnated clothing reduces the risk of bites. In addition, the burning of insect coils, sleeping under insecticide-treated bed nets and ceiling fans, along with mosquito screens on the doors and windows, provide additional protection (DOH, 2018; WHO, 2021). However, one needs to remain cautious of novel and non-certified methods of preventing mosquito bites which are

flooding the market, as these may create a misleading sense of protection (van Zyl, 2016).

4.7 Efficacy of Mosquito Repellents in Johannesburg, South Africa

4.7.1 Mosquito repellent efficacy

Personal protective measures are of paramount importance in the control of vector borne diseases. The use of mosquito repellents is an effective and additional tool for personal protection against the mosquitoes (Ogillo et al., 2016). Today there are numerous commercially marketed repellents that claim varying degrees of protection against mosquito bites; however, for most of these their claim of protective efficacy has not been scientifically verified (Section 1.5).

In this study, the protective efficacy of fifteen commercially marketed repellent products displayed excellent repellency, over a period of one hour, their percentage repellency ranged from 99.45% to 97.50% when tested against five-to-seven-day old female *An. gambiae* mosquitoes that had been starved of a blood meal but were sugar-fed (Table 3.19). Of these fifteen repellent products, the citronella oil-based repellent product, Medi-scabiol™ soap provided the highest level of protection (99.45 ± 0.28%). This is an interesting finding as plant-based repellents are favoured by many consumers as these are perceived to be safer and as effective as the long-established synthetic repellent products (Maia and Moore, 2011). The advantage of a plant-based product possessing good repellent properties is a favourable outcome for both the researchers and consumers, as such products are considered safe and eco-friendly (Rehman et al., 2014).

Plant-based repellent products have been in use since time immemorial. More especially in traditional ways in the tropics, and indeed by some communities in North America and Europe (Maia and Moore, 2011). Citronella oil is one of the plant extracts that has been proven to an effective mosquito repellent. Apart from the repellent effect, it was also reported to be both an irritant and toxic to the mosquitoes (Deletre et al., 2013a; Trongtokit et al., 2005b). In this research study, the citronella oil has been proven to be an effective and reliable repellent for short term protection against the mosquito bites for an hour period, which matches that found by Thorsell et al. (1998), Trongtokit et al. (2005a) and Harismah et al. (2017). Some studies have shown the citronella oil can provide a longer protection period against mosquito bites for up to two hours (Trongtokit et al., 2005b; Lee, 2018). However, in contrast, a lower efficacy of

citronella-based repellent product was also previously reported by Fradin and Day 2002) in a laboratory study conducted in United State. The ability to directly compare these products is fundamentally flawed as the manufacturer, in the majority of products, does not stipulate the exact percentage of citronella oil included in the product or the source of the oil. The latter is important to know as many factors can affect the composition of the oil and thereby altering the efficacy as a repellent. Factors include country, season plant harvested, process in which oil was obtained, ie distillation versus extraction (Kamatou et al, 2008).

In this study, the efficacy of citronella-based repellent was found to be statistically equal to that of DEET for short-term protection (Misni et al., 2017; Omar and Vythilingam, 2002). However, the poor stability of citronella oil due to it higher volatility and need for frequent applications still makes DEET, the gold standard repellent product, with a protection time of about 360 minutes (Diaz, 2016a; Trongtokit et al., 2005b).

The only wearable device tested was Mosquito patch™ and it is one of the three least effective products found in this assay. Although the active ingredient of this tested wearable device was Citronella which has proven repellent activity over an hour period (Table 3.19). This indicate the reason for the low effectiveness of the wearable devices might be attributed to low concentration of the emitted active ingredient at a particular time and this finding confirmed the result of a previously published study by Rodriguez et al. 2017) from their laboratory assay on a similar repellent's products.

The 'Anti-mozzie camping outdoor and indoor' cream was the second most active repellent product in this study and again it is a natural product containing citronella oil as the main ingredient that is combined with lemon grass oils, which is also a well-documented insect repellent (Table 3.19)(Agrawal et al., 2017).

The Mosquito Guard™, a PMD-based repellent product, displayed excellent protection against the *An. gambiae* mosquitoes. In this study, it was also found to be equally as effective as DEET for a period of one hour (Table 3.19) (Govere et al., 2000b; Moore et al. 2002). Interestingly, in some studies, PMD was reported to provide even more protections than DEET (Moore et al., 2002; Diaz, 2016b; Carroll et al., 2019).

From the results of this study, the South African public can be scientifically advised for an informed decision on the choice of a safe and effective repellent product. The natural products: Medi-Scabiol™ soap, Antimozie™ camping indoor and outdoor

cream, the pure beginning organic spray and Mylol™ perfumed repellent stick can be used for a short personal protection from mosquito bites. But needs to be regularly applied to ensure optimal protection over a long period being outside. While the Tabard™ DEET based products and Mosquito Guard™ PMD based products can be used for a long-term protection as reported in some previously published studies that were ran for a longer period than this study (Rodriguez et al., 2017; Feuser et al., 2020)

4.7.2 Spatial activity index (SAI)

Spatial repellency refers to the ability of volatile mosquito repellents to diffuse in the air to deter female *Anopheles* mosquitoes from entering the space around the susceptible host and as such prevent the host from being bitten (Norris and Coats, 2017). A spatial repellent is an alternative approach to the use of a contact repellent. The SAI is the measure of the movement of the mosquitoes away from the human odour in the present of the mosquito repellent, it is a measure used to determine the spatial repellence of a repellent chemical (O'Neal et al., 2019; WHO, 2013).

Nine of the tested repellent products displayed some form of spatial repellence (Table 3.20). The repellent with the highest spatial repellence was All-natural Guard™ product which is a natural mosquito repellent made from plant extracts, comprising of 750mg of *Chrysanthemum cineriae* folium and 6900mg *Azadirahta indica* extract. The repellent and irritant effects of these plants have previously demonstrated by Deletre et al. (2013b). Whilst Mosquito Guard™ containing PMD was shown to have a SAI of 0.15 ± 0.03 indicating it could be used as spatial repellent, as demonstrated by Menger et al. (2014) using a push-pull system to reduce house entry of malaria mosquitoes.

Presently most spatial repellents are in the form of a mosquito coils containing a pyrethroid (Ogoma et al., 2012). Pyrethroid is proposed to inhibit insect behaviour not through targeting the voltage gated sodium channel, but instead inhibiting the response of an odorant receptors to attractants in a similar way to PMD and nepetalactone Ogoma et al., 2012; Bohbot et al., 2011). In contrast, DEET-containing products (Tabard™) were found to be weakly attractant with a SAI of -0.03 ± 0.11 (Table 3.20). When compared with it overall percentage protection of 99.14 ± 0.87%, this shows that DEET is a good contact repellent and poor spatial repellent. This corroborates the observations by Bernier et al. (2005) on the spatial repellence of DEET and nepetalactone, an essential component of catnip oil.

The ideal compound repellent compound would be one that could have spatial repellency along with adulticidal properties, thereby interrupting the life cycle of the parasite and decreasing the transmission of malaria. The adulticidal properties of these commercially available products would need to be evaluated to fully assess the effectiveness in interrupting the transmission of malaria.

4.8 Limitations

4.8.1 Part one - Cross sectional survey

The main limitation of the Part one of this cross-sectional survey, was low representation of the public respondents from both countries due to the difficulty of getting data from them. This was mainly due to the stigma of paper sharing following the onset of the Covid-19 pandemic when not enough information was known on transmission of the virus.

4.8.2 Part two - Repellent efficacy assay

The main limitation of the Part two efficacy assays was the duration of the experiment, which was conducted for only an hour period. This is due to the difficulty in getting volunteers that will stay for a longer period, hence the percentage protections of this repellent were assessed for only one hour and this study cannot predict the highest duration of protection of the tested repellent products.

CHAPTER FIVE:

CONCLUSIONS

Appropriate malaria-related knowledge of targeted communities on malaria preventive measures and mosquito behaviours, like it breeding sites, is critical for a successful malaria control programme (Teklemariam, 2018). Good malaria-related knowledge along with a positive attitude on malaria will maximum the outcome of any planned malaria interventional program (Teklemariam, 2018). The government needs the support of the public and HCPs to “beat malaria”. Even if all possible malaria control tools are provided, these can only be effective with an active community involvement and their empowerment with malaria-related knowledge (Adedotun et al., 2010).

To the best of my knowledge this is the first study that compared the malaria-related knowledge and prevention between South Africa and Nigeria. The differences observed can serve as a learning point especially for the Nigerian policy makers to learn from the South African malaria control and elimination strategies through an increased malaria-related health promotion activity, to increase the awareness of the citizens about malaria and preventive measures.

Despite the good knowledge of the HCPs on management of malaria and their adherence to the treatment guideline, further insight is required as to whether the choice of first line medications to treat and prevent malaria stem from personal experiences in the clinical setting or when taking the medication themselves. In addition, clarify needs to be sought as to when last the HCPs were informed of the latest malaria prevention and treatment guidelines to correlate this to their slightly outdated choices of using quinine as the first-line agent to treat mild to moderate malaria. This re-enforces the recommendation for continued education through seminars for the HCPs in both countries and through all forms of multimedia to reach the public to address some noted misconceptions.

By further educating all population groups in both countries, additional prevention and control measures could become more familiar to communities and be used in conjunction with LLINs, such as IRS, health promotion and case management. Through workshops and media, the importance of removing breeding sites to prevent mosquitoes from breeding and continuing the life cycle of malaria, would be essential. Education could ensure many in the communities are more aware of the dangers of

malaria such that they seek medical attention within 24 hours of presenting with malaria symptom and decrease the mortality rate in our two countries.

In the second part of this study, insect repellents were investigated. To the best of my knowledge, this is the first survey that collate all the mosquito repellent products sold in Johannesburg, South Africa. This study had supported the academia in the field of malaria with some malariotomeric indices from two geographically distinct countries (South Africa and Nigeria).

The online and market survey revealed almost one hundred different repellent products sold in Johannesburg, South Africa. The online purchase of the repellents was found to be higher than the market purchase of the mosquito repellent products. However, only slightly more than half of this products was found to be approved by the South African Health Products Regulatory Authority (SAHPRA). Most of the surveyed products were plant based with citronella oil being the most common active ingredient seen in most of the products.

Despite the good efficacy of all fifteen repellent products tested for a short period of personal protection from mosquito bites, it will be necessary to lengthen the testing time to ascertain their long-term protection. Finally, it is well documented that providing an efficient malaria-related health education to the communities in malaria endemic areas, will improve their understanding of malaria, and improve their attitude on malaria prevention which may lead to malaria control and elimination from the country (Al-Adhroey et al., 2010). Hence, the results of this study can serve as a guidance for the citizens of South Africa and Africa on the choice of a safe and effective repellent product.

Education is key to ensuring the public and HCPs are continuously reminded and updated on the methods to prevent malaria as well as treat an infection. By using a multimedia approach to reach the masses, it will support any government initiatives to stop malaria transmission and end malaria cases in the country. But complacency by the public and the government should be warned against to ensure all fundamental actions are taken and the government provides constant un waivered support to these programs.

CHAPTER SIX:

REFERENCES

Abate, A., Degarege, A. & Erko, B. 2013. Community knowledge, attitude and practice about malaria in a low endemic setting of Shewa Robit town, Northeastern Ethiopia. *BMC Public Health,* 13**,** 1-8.

Abdalla , Z. A., Rahma, N. A., Hassan, E. E., Abdallah, T. M., Hamad, H. E., Omer, S. A. & Adam, I. 2019. The diagnostic performance of rapid diagnostic tests and microscopy for malaria diagnosis in Eastern Sudan using a nested polymerase chain reaction assay as a reference standard. *Transactions of The Royal Society of Tropical Medicine and Hygiene,* 13**,** 701-705.

Abdulkareem, B. O., Adam, A. O., Ahmed, A. O., Mariam, A. A. & Samuel, U. U. 2017. Malaria-induced anaemia and serum micronutrients in asymptomatic *Plasmodium falciparum* infected patients. *Journal of Parasitic Diseases,* 41**,** 1093-1097.

Adedotun, A., Morenikeji, O. & Odaibo, A. 2010. Knowledge, attitudes and practices about malaria in an urban community in South-Western Nigeria. *Journal of Vector Borne Diseases,* 47**,** 155-161.

Adiel, T., Chessed, G., Buduwara, J., Sami, R. & Tafem, M. 2021. Knowledge, attitudes and practices on malaria in farming communities of Lau local government area of Taraba State Nigeria. *South Asian Journal of Parasitology***,** 16-23.

Adigun, A. B., Gajere, E. N., Oresanya, O. & Vounatsou, P. 2015. Malaria risk in Nigeria: Bayesian geostatistical modelling of 2010 malaria indicator survey data. *Malaria Journal,* 14**,** 1-8.

Afaya, A., Salia, S. M., Opare, F. Y., Ali, S. & Afaya, R. A. 2017. Patients' adherence to antimalarial medication; self-report of patients at the volta regional hospital, Ghana. *International Journal of Research in Medical Sciences,* 5**,** 4234-4241.

Afify, A., Betz, J. F., Riabinina, O., Lahondère, C. & Potter, C. J. 2019. Commonly used insect repellents hide human odors from *Anopheles* mosquitoes. *Current Biology,* 29**,** 3669-3680.

Afolabi, O. J., Akinneye, J. O. & Igiekhume, A. M. A. 2019. Identification, abundance, and diversity of mosquitoes in Akure South Local Government Area, Ondo State, Nigeria. *The Journal of Basic and Applied Zoology,* 80**,** 39-45.

Agrawal, N., Maddikeri, G. L. & Pandit, A. B. 2017. Sustained release formulations of citronella oil nanoemulsion using cavitational techniques. *Ultrasonics Sonochemistry,* 36**,** 367-374.

Aguiar, L., Machado, M., Sanches-Vaz, M., Prudêncio, M., Vale, N. & Gomes, P. 2019. Coupling the cell-penetrating peptides transportan and transportan 10 to primaquine enhances its activity against liver-stage malaria parasites. *Medicinal Chemistry Communications,* 10**,** 221-226.

Ahir, G. & Bala, D. 2012. Perceptions and attitudes of resident doctors about malaria treatment as per national drug policy on malaria. *National Journal of Community Medicine,* 3**,** 71-73.

Ajao, A. M., Idris, N., Sunday, O. J., Popoola, N. A., Oladipo, S. O. & Ladipo, E. F. 2017. Knowledge, attitude and practices about malaria among members of a university community in Kwara State, Nigeria. *Animal Research International,* 14**,** 2793-2803.

Ajonina, M. U., Ware, K. B., Ngonga, D. B., Abong, R. A., Nfor, C. K. & Apinjoh, T. O. 2019. Malaria perceptions among medicine vendors in Buea community: An assessment of knowledge of malaria and conditions of antimalarial drug dispensing. *Innovations In Pharmacy,* 10**,** 7-7.

Aju-Ameh, C. O., Awolola, S. T., Mwansat, G. S. & Mafuyai, H. B. 2016. Malaria related knowledge attitude and practices (MKAP) in fourteen communities in Benue State North Central Nigeria: Evidence for the success of focal malaria control intervention programmes. *International Journal Of Mosquito Research,* 55**,** 11-16.

Akogun, O. B. 2008. *A study on presumptive diagnosis and home management of childhood malaria among nomadic Fulani In Demsa, Nigeria.* University of the Western Cape. http://etd.uwc.ac.za/xmlui/bitstream/handle/11394/2817/Akogun_MPA_2008.pdf;sequence=1 [Accessed17/01/ 2022]

Al-Adhroey, A. H., Nor, Z. M., Al-Mekhlafi, H. M. & Mahmud, R. 2010. Opportunities and obstacles to the elimination of malaria from Peninsular Malaysia: Knowledge, attitudes and practices on malaria among aboriginal and rural communities. *Malaria Journal,* 9**,** 137-142.

Alake, M. 2020. *What exactly is the age of consent in Nigeria? [Explainer]* [Online]. Available: https://www.pulse.ng/news/local/the-nigerian-age-of-consent-is-18-not-11/0zs6h4h [Accessed 3/07/ 2022].

Alawode, O., Chima, V. & Awoleye, A. 2019. Household characteristics as determinants of ownership of mosquito nets in urban households in Nigeria. *Scientific African,* 6**,** e00156-e00175.

Al-Shehri, H., Power, B. J., Archer, J., Cousins, A., Atuhaire, A., Adriko, M., Arinaitwe, M., Alanazi, A. D., LaCourse, E. J., Kabatereine, N. B., et al. 2019. Non-invasive surveillance of *Plasmodium* infection by real-time PCR analysis of ethanol preserved faeces from Ugandan school children with intestinal schistosomiasis. *Malaria Journal,* 18**,** 109-116.

Amadi, E., Harry, S. & Ogbalu, O. 2015. Prelimnary survey on the abundance of mosquito species and transmission of *Plasmodium* to humans in Bille, Oporoama, Sama and Tema communities of rivers state, Nigeria. *International Organization Of Scientific Research Journal Of Pharmacy And Biological Sciences,* 10**,** 82-86*,* 10**,** 82-86.

Amaechi, E. C., Ukpai, O. M., Ohaeri, C. C., Irole-Eze, O. P., Ejike, B. U., Ihemanma, C. A., Okorocha, A. N., Egwu, O. & Nwadike, C. C. 2018. Knowledge and practices towards malaria control and prevention in an irrigated community, north central nigeria. *Annales Of West University Of Timisoara. Series of Biology,* 21**,** 175-184.

Amer, A. & Mehlhorn, H. 2006. Repellency effect of forty-one essential oils against *Aedes, Anopheles, and Culex* mosquitoes. *Parasitology Research,* 99**,** 478-490.https://doi.org/10.1007/s00436-006-0184-1.

Amimo, F., Moon, T. D., Magit, A., Sacarlal, J., Lambert, B. & Nomura, S. 2019. Trends in comparative efficacy and safety of malaria control interventions for maternal and child health outcomes in Africa: A study protocol for a Bayesian network meta-regression exploring the effect of HIV and malaria endemicity spectrum. *British Medical Journal,* 9**,** e024313-e024324.

Amir, A., Cheong, F.-W., De Silva, J. R. & Lau, Y.-L. 2018. Diagnostic tools in childhood malaria. *Parasites & Vectors,* 11**,** 53-65.

Amusan, V. O., Umar, Y. A. & Vantsawa, P. A. 2017. Knowledge, attitudes and practices on malaria prevention and control among private security guards within

Kaduna Metropolis, Kaduna State-Nigeria. *Science Journal of Public Health,* 5**,** 240–245.

Amzat, J. 2011. Assessing the progress of malaria control in Nigeria. *World Health Population,* 12**,** 42-51.

Andegiorgish, A. K., Kidane, E. A., Welday, B. E., Weldekidan, M. W., Tekle, N. Y. & Sibahtu, L. F. 2019. Knowledge, attitude and treatment seeking behavior for malaria in may-aynee administration, eritrea. *Biomedical Journal of Scientific & Technical Research,* 22**,** 16393–16399.

Anumudu, C., Adepoju, A., Adediran, M., Adeoye, O., Kassim, A., Oyewole, I. & Nwuba, R. 2006. Malaria prevalence and treatment seeking behaviour of young nigerian adults. *Annals of African Medicine,* 5**,** 82-88.

Arsic, B., Barber, J., Čikoš, A., Mladenovic, M., Stankovic, N. & Novak, P. 2018. 16-membered macrolide antibiotics: A review. *International Journal of Antimicrobial Agents,* 51**,** 283-298.

Asadollahi, A., Khoobdel, M., Zahraei-Ramazani, A., Azarmi, S. & Mosawi, S. H. 2019. Effectiveness of plant-based repellents against different *Anopheles* species: A systematic review. *Malaria Journal,* 18**,** 436-455.

Atting, I., Ekpo, N., Akpan, M., Bassey, B., Asuquo, M., Usip, L., Inyama, P. & Samdi, L. 2019. Insecticide susceptibility profile of malaria vector populations from the coastal and mainland areas of Akwa Ibom State, Nigeria. *Journal Of Advances In Medicine And Medical Research***,** 1-11.

AVIDBRANDS. 2020. *Onguard pump spray 150ml* [Online]. Available: https://avidbrands.co.za/product/onguard-pump-spray-150ml/ [Accessed 26/04/ 2020].

Awolola, T. S., Adeogun, A., Olakiigbe, A. K., Oyeniyi, T., Olukosi, Y. A., Okoh, H., Arowolo, T., Akila, J., Oduola, A. & Amajoh, C. N. 2018. Pyrethroids resistance intensity and resistance mechanisms in *Anopheles gambiae* from malaria vector surveillance sites in Nigeria. *PLoS One,* 13**,** e0205230-e0205240.

Babalola, C. P. 2013. Experimental determination of the physicochemical properties of lumefantrine. *African Journal of Medicine and Medical Sciences,* 42**,** 209-214.

Balaji, A. P. B., Ashu, A., Manigandan, S., Sastry, T. P., Mukherjee, A. & Chandrasekaran, N. 2017. Polymeric nanoencapsulation of insect repellent: Evaluation of its bioefficacy on *Culex quinquefasciatus* mosquito population and

effective impregnation onto cotton fabrics for insect repellent clothing. *Journal of King Saud University - Science,* 29**,** 517-527.

Balamurugesan, K., Davis, P., Ponprabha, R. & Sarasveni, M. 2019. Chloroquine induced urticaria: A newer adverse effect. *Journal of Family Medicine And Primary Care,* 8**,** 2545-2552.

Bamiselu, O. F., Ajayi, I., Fawole, O., Dairo, D., Ajumobi, O., Oladimeji, A. & Steven, Y. 2016. Adherence to malaria diagnosis and treatment guidelines among healthcare workers in Ogun State, Nigeria. *Biomed Central Public Health,* 16**,** 828-837.

Banggood. 2006. USB charging electric mosquito repellent constant temperature heating indoor mosquito dispeller [Online]. Available: https://www.banggood.com/USB-Charging-Electric-mosquito-Repellent-Constant-Temperature-Heating-Indoor-Mosquito-Dispeller-p-1528799.html?gmcCountry=ZA&currency=ZAR&createTmp=1&utm_source=googleshopping&utm_medium=cpc_bgs&utm_content=xibei&utm_campaign=xibei-ssc-za-all-newcustom-0904-13anv&gclid=Cj0KCQiA0ZHwBRCRARIsAK0Tr-pEZ__phE-RSS8qyS9SNPIWuoe0-zHL_eW3PxBCjoS2LUPe_IjRe4AaAq-JEALw_wcB&cur_warehouse=CN [Accessed 26/12/ 2019].

Banggood. 2018. *UV light pest repeller electronic repellent plug pests control mosquito dispeller - white* [Online]. Available: https://www.banggood.com/UV-Light-Pest-Repeller-Electronic-Repellent-Plug-Pests-Control-Mosquito-Dispeller-p-1347452.html?gmcCountry=ZA&currency=ZAR&createTmp=1&utm_source=googleshopping&utm_medium=cpc_bgs&utm_content=xibei&utm_campaign=xibei-ssc-za-all-newcustom-0904-13anv&gclid=CjwKCAiAuqHwBRAQEiwAD-zr3fA3uLxCp1Ej9JimWSWVHgNCh7NszU22zOGqC05M715oWF9iS_UH-xoCJP8QAvD_BwE&ID=233&cur_warehouse=CN [Accessed 29/12/ 2019].

Baranauskienė, R., Bendžiuvienė, V., Ragažinskienė, O. & Venskutonis, P. R. 2019. Essential oil composition of five nepeta species cultivated in lithuania and evaluation of their bioactivities, toxicity and antioxidant potential of hydrodistillation residues. *Food and Chemical Toxicology,* 129**,** 269-280.

Barat, L. M., Palmer, N., Basu, S., Worrall, E., Hanson, K. & Mills, A. 2004. Do malaria control interventions reach the poor? A view through the equity lens. *American Journal of Tropical Medicine and Hygiene,* 71**,** 174-178.

Beri, G. C. 2009. *Concepts & Theories of Attitude* [Online]. Tata: Mc-GrawHill. Available: https://shodhganga.inflibnet.ac.in/bitstream/10603/167789/9/09_chapter%202.pdf [Accessed 6/4/2022].

Berna, A. Z., McCarthy, J. S., Wang, R. X., Saliba, K. J., Bravo, F. G., Cassells, J., Padovan, B. & Trowell, S. C. 2015. Analysis of breath specimens for biomarkers of *Plasmodium falciparum* infection. *The Journal of Infectious Diseases,* 212**,** 1120-1128.

Bernier, U. R., Furman, K. D., Kline, D. L., Allan, S. A. & Barnard, D. R. 2005. Comparison of contact and spatial repellency of catnip oil and N, N-Diethyl-3-methylbenzamide (deet) against mosquitoes. *Journal of Medical Entomology,* 42**,** 306-311.

Beyene, H. B., Telele, N. F. & Mekuria, A. H. 2015. Knowledge, attitude and practice on malaria and associated factors among residents in Pawe District, North West Ethiopia: A cross-sectional study. *Science Journal of Public Health,* 3**,** 303-309.

Bezerra, F. M., Lis, M., Carmona, Ó. G., Carmona, C. G., Moisés, M. P., Zanin, G. M. & Moraes, F. F. 2019. Assessment of the delivery of citronella oil from microcapsules supported on wool fabrics. *Powder Technology,* 343**,** 775-782.

Bhagat, K. & Nyazema, N. 2001. General practitioners and clinical guidelines. *East African Medical Journal,* 78**,** 30-34.

Bhatt, S., Weiss, D. J., Cameron, E., Bisanzio, D., Mappin, B., Dalrymple, U., Battle, K. E., Moyes, C. L., Henry, A., Eckhoff, P. A., et al. 2015. The effect of malaria control on *Plasmodium falciparum* in Africa between 2000 and 2015. *Nature,* 526**,** 207-211.

Biddau, M. & Sheiner, L. 2019. Targeting the apicoplast in malaria. *Biochemical Society Transactions,* 47**,** 973-983.

Birhanie, M. 2016. Comparison of partec rapid malaria test with conventional light microscopy for diagnosis of malaria in Northwest Ethiopia. *Journal of Parasitology Research,* 2016**,** 1-5.

Birkett, M. A., Hassanali, A., Hoglund, S., Pettersson, J. & Pickett, J. A. 2011. Repellent activity of catmint, *Nepeta cataria*, and iridoid nepetalactone isomers against afro-tropical mosquitoes, ixodid ticks and red poultry mites. *Phytochemistry,* 72**,** 109-114.

BlueToothMouseTech. 2020. *Ultrasonic mosquito repellent bracelets armband* [Online]. Available: http://www.bluetoothmousetech.com/ultrasonic-mosquito-repellent-bracelets-armband?___store=za [Accessed 26/04/ 2020].

Bohbot, J., Fu, L., Le, T., Chauhan, K., Cantrell, C. & Dickens, J. 2011. Multiple activities of insect repellents on odorant receptors in mosquitoes. *Medical and Veterinary Entomology,* 25**,** 436-444.

Boukoumba, F. M., Lekana-Douki, J. B., Matsiegui, P. B., Moukodoum, D. N., Adegnika, A. A. & Oyegue-Liabagui, S. L. 2021. High prevalence of genotypes associated with sulfadoxine/pyrimethamine resistance in the rural area of Fougamou, Gabon. *Journal of Global Antimicrobial Resistance,* 25**,** 181-186.

Brasil, P., Zalis, M. G., de Pina-Costa, A., Siqueira, A. M., Júnior, C. B., Silva, S., Areas, A. L. L., Pelajo-Machado, M., de Alvarenga, D. A. M., da Silva Santelli, A. C. F., et al. 2017. Outbreak of human malaria caused by *Plasmodium simium* in the Atlantic Forest in Rio De Janeiro: A molecular epidemiological investigation. *The Lancet Global Health,* 5**,** e1038-e1046.

Brooke, B., Kloke, G., Hunt, R., Koekemoer, L., Tem, E., Taylor, M., et al. 2001. Bioassay and biochemical analyses of insecticide resistance in southern African *Anopheles funestus* (Diptera: Culicidae). *Bulletin of Entomological Research,* 91**,** 265-272.

Brooke, B., Koekemoer, L., Kruger, P., Urbach, J., Misiani, E. & Coetzee, M. 2013. Malaria vector control in South Africa. *2013,* 103**,** 784-788.

BSCHOLARLY. 2022. *Countries with the best education system in Africa 2022: Top 10* [Online]. Available: https://bscholarly.com/countries-with-the-best-education-system-in-africa/ [Accessed 17/01/ 2022].

Burke, A. M., Brooke, B. D. & Duncan, F. D. 2019b. Metabolic rate does not vary with seasonal change in *Anopheles arabiensis* adults in South Africa. *Journal of Insect Physiology,* 118**,** 103942-103948.

Burke, A., Dahan-Moss, Y., Duncan, F., Qwabe, B., Coetzee, M., Koekemoer, L. & Brooke, B. 2019a. *Anopheles parensis* contributes to residual malaria transmission in South Africa. *Malaria Journal,* 18**,** 1-7.

Burke, A., Dandalo, L., Munhenga, G., Dahan-Moss, Y., Mbokazi, F., Ngxongo, S., Coetzee, M., Koekemoer, L. & Brooke, B. 2017. A new malaria vector mosquito in South Africa. *Scientific Reports,* 7**,** 1-5.

Bynum, B. 2008. *A history of malaria* [Online]. Available: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(08)60612-1/fulltext [Accessed 9622 371].

C V. O., Umar, Y. A. & Vantsawa, P. A. 2017. Knowledge, attitudes and practices on malaria prevention and control among private security guards within Kaduna Metropolis, Kaduna State-Nigeria. *Science Journal Of Public Health,* 5**,** 240–245.

CapeUnionmart. 2020a. *BuggerOff Soap 100g* [Online]. Available: https://www.capeunionmart.co.za/products/buggeroff-soap-100g/113474-0000.html [Accessed 24/04/ 2020].

CapeUnionmart. 2020b. *HHL Vital Protection 100ml AM2* [Online]. Available: https://www.capeunionmart.co.za/products/hhl-vital-protection-100ml-am2/109861-0000.html [Accessed 24/04/ 2020].

CapeUnionmart. 2020c. *Insect Repellents* [Online]. Available: https://www.capeunionmart.co.za/c/gear-health-repellents/ [Accessed 08/04/ 2022].

CapeUnionmart. 2020d. *Sea To Summit Citronella Wilderness Wash 89ml* [Online]. Available: https://www.capeunionmart.co.za/products/sea-to-summit-citronella-wilderness-wash-89ml/102113-0000.html [Accessed 24/04/ 2020].

Carroll, S. P., Venturino, J. & Davies, J. H. 2019. A milestone in botanical mosquito repellents: Novel pmd-based formulation protects more than twice as long as high-concentration deet and other leading products. *Journal of the American Mosquito Control Association,* 35**,** 186-191.

CDC. 2017. *Update: South Africa: Limpopo, North West, and Gauteng provinces* [Online]. Available: https://www.cdc.gov/malaria/new_info/2017/South_Africa_2017.htm [Accessed 07/05/ 2020].

CDC. 2018. *Updated cdc recommendations for using artemether-lumefantrine for the treatment of uncomplicated malaria in pregnant women in the United States* [Online]. Available: https://www.cdc.gov/mmwr/volumes/67/wr/mm6714a4.htm?s_cid=mm6714a4_w [Accessed 30/10/ 2019].

CDC. 2021. *Malaria information and prophylaxis, by country [n]* [Online]. Available: https://www.cdc.gov/malaria/travelers/country_table/n.html [Accessed 10/01/ 2022].

Census, S. S. A. 2004. *Gauteng provincial profile 2004* [Online]. Pretoria 0001 Statistics South Africa, Private Bag X44,. Available: http://www.statssa.gov.za/publications/Report-00-91-07/Report-00-91072004.pdf [Accessed 23/04/ 2019].

Cerceau, C. I., Barbosa, L. C. A., Alvarenga, E. S., Maltha, C. R. A. & Ismail, F. M. D. 2020. 1H-NMR and GC for detection of adulteration in commercial essential oils of *Cymbopogon* ssp. *Phytochemical Analysis,* 31**,** 88-97.

Chanquia, S. N., Larregui, F., Puente, V., Labriola, C., Lombardo, E. & Liñares, G. G. 2019. Synthesis and biological evaluation of new quinoline derivatives as antileishmanial and antitrypanosomal agents. *Bioorganic Chemistry,* 83**,** 526-534.

Charpentier, E., Benichou, E., Pagès, A., Chauvin, P., Fillaux, J., Valentin, A., Guegan, H., Guemas, E., Salabert, A. S., Armengol, C., et al. 2019. Performance evaluation of different strategies based on microscopy techniques, rapid diagnostic test and molecular loop-mediated isothermal amplification assay for the diagnosis of imported malaria. *Clinical Microbiology and Infection,* 26**,** 115-121.

Chen-Hussey, V., Behrens, R. & Logan, J. G. 2014. Assessment of methods used to determine the safety of the topical insect repellent N, N-diethyl-m-toluamide (deet). *Parasites & Vectors,* 7**,** 173-179.

Chico, M. & Ter Kuile, F. O. 2018. Back to chloroquine for malaria prophylaxis in pregnancy? *The Lancet Infectious Diseases,* 18**,** 1-4.

Chigurupati, P. & Srinivas, M. 2016. Quantitative buffy coat technique in the diagnosis of malarial parasites: A cost-effective method. *Parasitologists United Journal,* 9**,** 55-58.

Christian, R., Dahan-Moss, Y., Braack, L., Munhenga, G., Kaiser, M., Lobb, L., Wood, O., Erlank, E., Tshikae, P. & Burke, A. 2018. Malaria vector surveillance report, South Africa, January–December, 2017. *NICD Public Health Surveillance Bulletin,* 16**,** 29-35.

Chu, X.-M., Wang, C., Liu, W., Liang, L.-L., Gong, K.-K., Zhao, C.-Y. & Sun, K.-L. 2019. Quinoline and quinolone dimers and their biological activities: An overview. *European Journal of Medicinal Chemistry,* 161**,** 101-117.

Chukwuocha, U. 2012. Malaria control in Nigeria. *Primary Health Care,* 2**,** 2167-1079.1000118.

Coetzee, M., Kruger, P., Hunt, R., Durrheim, D., Urbach, J. & Hansford, C. 2013. Malaria in South Africa: 110 years of learning to control the disease. *South African Medical Journal,* 103**,** 770-778.

Conrad, M. D. & Rosenthal, P. J. 2019. Antimalarial drug resistance in Africa: The calm before the storm? *The Lancet Infectious Diseases,* 19**,** e338-e351.

ConstitutionofSouthAfrica. 1996. *South African government* [Online]. Available: https://www.gov.za/documents/constitution/constitution-republic-south-africa-1996-1 [Accessed 16/01/ 2022].

Corrêa, A. P. S. A., Galardo, A. K. R., Lima, L. A., Câmara, D. C. P., Müller, J. N., Barroso, J. F. S., et al. 2019. Efficacy of insecticides used in indoor residual spraying for malaria control : an experimental trial on various surfaces in a “test house”. *Malaria Journal,* 18**,** 345-358.

Costa, M. R. F., Barcelos, A. L. R., Camargo, M. a. D., Melo, G. C. D., Almeida, A. C., Costa, A. G. D., et al. 2019. Performance of an immuno-rapid malaria Pf/Pv rapid diagnostic test for malaria diagnosis in the Western Brazilian Amazon. *Revista Da Sociedade Brasileira De Medicina TropicaL,* 52**,** 1-5.

Cox-Singh, J., Davis, T. M. E., Lee, K. S., Shamsul, S. S. G., Matusop, A., Ratnam, S., et al. 2008. *Plasmodium knowlesi* Malaria in Humans Is Widely Distributed and Potentially Life Threatening. *Clinical Infectious Diseases,* 46**,** 165-171.

Dandalo, L. C., Brooke, B. D., Munhenga, G., Lobb, L. N., Zikhali, J., Ngxongo, S. P., et al. 2017. Population Dynamics and *Plasmodium falciparum* (Haemosporida: Plasmodiidae) Infectivity Rates for the Malaria Vector *Anopheles arabiensis* (Diptera: Culicidae) at Mamfene, KwaZulu-Natal, South Africa. *Journal Of Medical Entomology,* 54**,** 1758-1766.

Darteh, E. K. M., Buabeng, I. & Akuamoah-Boateng, C. 2020. Uptake of intermittent preventive treatment in pregnancy for malaria: Further analysis of the 2016 ghana malaria indicator survey. *Journal of Public Health,* 29**,** 967–978.

Das, S., Jang, I. K., Barney, B., Peck, R., Rek, J. C., Arinaitwe, E., et al. 2017. Performance of a High-Sensitivity Rapid Diagnostic Test for *Plasmodium falciparum* Malaria in Asymptomatic Individuals from Uganda and Myanmar and Naive Human Challenge Infections. *The American Journal Of Tropical Medicine And Hygiene,* 97**,** 1540-1550.

Dawaki, S., Al-Mekhlafi, H. M., Ithoi, I., Ibrahim, J., Atroosh, W. M., Abdulsalam, A. M., et al. 2016. Is Nigeria winning the battle against malaria? Prevalence, risk factors and KAP assessment among Hausa communities in Kano State. *Malaria Journal,* 15**,** 351-364.

DeBaun, M. R., Galadanci, N. A. & Vichinsky, E. P. 2019. *Sickle cell disease in sub-Saharan Africa* [Online]. Wolters Kluwer UpToDate. Available: https://www.uptodate.com/contents/sickle-cell-disease-in-sub-saharan-africa [Accessed 18/02/ 2020].

Deletre, E., Martin, T., Campagne, P., Bourguet, D., Cadin, A., Menut, C., et al. 2013. Repellent, irritant and toxic effects of 20 plants extracts on adults of the malaria vector *Anopheles gambiae* mosquito. *Public Library Of Science One,* 8**,** e82103-e82113.

Dennis, E. J. & Vosshall, L. B. 2018. DEET feet: *Aedes aegypti* mosquitoes use their tarsi to sense DEET on contact. *Bio-Archive Journal***,** 360222-360245.

Dennis, E. J., Goldman, O. V. & Vosshall, L. B. 2019. *Aedes Aegypti* Mosquitoes Use Their Legs To Sense DEET On Contact. *Current Biology,* 29**,** 1551-1556.E5.

Depina, A. J., Dia, A. K., De Ascenção Soares Martins, A., Ferreira, M. C., Moreira, A. L., Leal, S. V., Et Al. 2019. Knowledge, Attitudes And Practices About Malaria In Cabo Verde : A Country In The Pre-Elimination Context. *Biomed Central Public Health,* 19**,** 850-863.

Diaz, J. H. 2016a. Chemical And Plant-Based Insect Repellents: Efficacy, Safety, And Toxicity. *Wilderness & Environmental Medicine,* 27**,** 153–163.

Diaz, J. H. 2016b. Chemical And Plant-Based Insect Repellents: Efficacy, Safety, And Toxicity. *Wilderness & Environmental Medicine,* 27**,** 153-163.

Dirk Van Der Berg, J., Duvenage, C. S. J., Roskell, N. S. & Scott, T. R. 1999. Safety And Efficacy Of Atovaquone And Proguanil Hydrochloride For The Prophylaxis Of *Plasmodium falciparum* Malaria In South Africa. *Clinical Therapeutics,* 21**,** 741-749.

Dischempharmacy. 2020a. *Citro-Cream With Citronella & Lemongrass Oil 500ml* [Online]. Available: Https://Www.Dischem.Co.Za/Citro-Cream-With-Citronella-Lemongrass-Oil-500ml [Accessed 25/04/ 2020].

Dischempharmacy. 2020b. *Citro Lotion 125ml* [Online]. Available: Https://Redcap.Core.Wits.Ac.Za/Redcap/Redcap_V9.7.8/Dataentry/Index.Php?Pid=11177&Page=My_First_Instrument&Id=70&Auto=1 [Accessed 25/04/ 2020].

Dischempharmacy. 2020c. *Dis-Chem Citronella Oil 20ml* [Online]. Available: Https://Www.Dischem.Co.Za/Dis-Chem-Citronella-Oil-20ml [Accessed 25/04/ 2020].

Dischempharmacy. 2020d. *Elektra Anti Mozz Lamp* [Online]. Available: Https://Www.Dischem.Co.Za/Elektra-Anti-Mozz-Lamp [Accessed 25/04/ 2020].

Dischempharmacy. 2020e. *Pigeon Anti Mosquito Baby Wipes 12's* [Online]. Available: https://www.dischem.co.za/pigeon-anti-mosquito-baby-wipes-12-s [Accessed 25/04/ 2020].

Dischempharmacy. 2020f. *Purity & Elizabeth Anne's Baby Insect Repellent Cream 50ml* [Online]. Available: https://www.dischem.co.za/elizabeth-anne-baby-insect-repellent-cream-50ml [Accessed 25/04/ 2020].

Dischempharmacy. 2020g. *Purity & Elizabeth Anne's Baby Insect Repellent Spray 125ml* [Online]. Available: https://www.dischem.co.za/elizabeth-anne-baby-insect-repellent-spray-125ml [Accessed 25/04/ 2020].

Dischempharmacy. 2020h. *Republic Umbrella Mosquito Guard Natural Aerosol 150ml 5hr* [Online]. Available: https://www.dischem.co.za/republic-umbrella-mosquito-gaurd-natural-aerosol-150ml-5hr [Accessed 25/04/ 2020].

Djouaka, R. J., Atoyebi, S. M., Tchigossou, G. M., Riveron, J. M., Irving, H., Akoton, R., Kusimo, M. O., Bakare, A. A. & Wondji, C. S. 2016. Evidence of a multiple insecticide resistance in the malaria vector *Anopheles funestus* in South West Nigeria. *Malaria journal,* 15**,** 1-10.

DrugBank. 2010. *Artemether* [Online]. Available: https://www.drugbank.ca/drugs/DB06697 [Accessed 13/11/ 2019].

DrugBank. 2015. *Artesunate* [Online]. Available: https://www.drugbank.ca/drugs/DB09274 [Accessed 10/11/ 2019].

Eden, W. T., Alighiri, D., Supardi, K. I. & Cahyono, E. 2020. The mosquito repellent activity of the active component of air freshener gel from java citronella oil (*Cymbopogon winterianus*). *Journal of Parasitology Research,* 2020**,** 1-5.

Edet-Utan, O., Ojediran, T., Usman, S. O., Akintayo-Usman, N. O., Fadero, T., Oluberu, O. A., et al. 2016. Knowledge, perception and practice of malaria management among non-medical students of higher institutions in Osun state, Nigeria. *American Journal Of Biotechnology Medical Research,* 1**,** 5-9.

Enayati, A., Hemingway, J. & Garner, P. 2007. Electronic mosquito repellents for preventing mosquito bites and malaria infection. *Cochrane database of systematic reviews***,** 1-14.

Espinoza, J. L. 2019. Malaria resurgence in the Americas: An underestimated threat. *Pathogens,* 8**,** 11-14.

Essentially Natural. 2020a. *Essentially natural bug off! - natural insect repellent* [Online]. Available: https://essentiallynatural.co.za/products/bug-off [Accessed 26/04/ 2020].

Essentially Natural. 2020b. *Essentially natural citronella essential oil* [Online]. Available: https://essentiallynatural.co.za/products/en-citronella-eo?pr_prod_strat=copurchase&pr_rec_pid=2092111233120&pr_ref_pid=2092051038304&pr_seq=uniform [Accessed 26/04/ 2020].

Esu, E. B., Effa, E. E., Opie, O. N. & Meremikwu, M. M. 2019. Artemether for severe malaria. *Cochrane Database of Systematic Reviews***,** 1-4.

Faidallah, H. M., Panda, S. S., Serrano, J. C., Girgis, A. S., Khan, K. A., Alamry, K. A., et al. 2016. Synthesis, antimalarial properties and 2D-QSAR studies of novel triazole-quinine conjugates. *Bioorganic And Medicinal Chemistry,* 24**,** 3527-3539.

Faithful to Nature. 2019. *Natural orange house hold insect repellent* [Online]. Available: https://www.faithful-to-nature.co.za/natural-orange-house-hold-insect-repellent?sfdr_ptcid=9581_617_272294805&sfdr_hash=203cb4267bdfc841d457f68ead8886b9&gclid=CjwKCAiAuqHwBRAQEiwAD-zr3cWAIMFXHuvpVao6UQ2qVvwGN8AoJu083tcjCKmUYWWfjnGCxM93shoC_VsQAvD_BwE [Accessed 29/12/ 2019].

Faithful to Nature. 2020. *Wild basil & lemongrass mosquito repellent victorian garden* [Online]. Available: https://www.faithful-to-nature.co.za/wild-basil-and-lemongrass-

mosquito-repellent?smplid=989&sfdr_ptcid=9581_617_81043959&sfdr_hash=9adea9f8b31f3dc13e3310c864b26aa6&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx_Cj6Bg8q00AXE9TpHUTeuaFA8Mno_BRuQSi-aao7S1GwJSG986jdEaAvPjEALw_wcB#250=2737 [Accessed 21/03/ 2020].

Faithful to Nature. 2020a. *Ananta luxury hand rolled incense - citronella, ananta* [Online]. Available: https://www.faithful-to-nature.co.za/ananta-luxury-hand-rolled-incense-citronella?sfdr_ptcid=9581_617_547317304&sfdr_hash=20e1d1db25f741ce2dff42e5071cd92f&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx9D1OPQmZyymJ-EZkXf2MUmS8lkNgON4C1_tcc6lgaY3oGzA_-KAnsaApRcEALw_wcB [Accessed 22/03/ 2020].

Faithful to Nature. 2020b. *Badger anti bug balm travel size, badger balm* [Online]. Available: https://www.faithful-to-nature.co.za/badger-anti-bug-balm-travel-size?sfdr_ptcid=9581_617_81065034&sfdr_hash=17f513166f4161eaeee50b43abfecae5&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx-e28p2m0DD5bzfCdL9TAiI3d3wvKfEqzKQusVFpkPuVfNnYETP-hcaAoXvEALw_wcB [Accessed 22/03/ 2020].

Faithful to Nature. 2020c. *Badger spf34 sunscreen & anti-bug balm for face & body, badger balm* [Online]. Available: https://www.faithful-to-nature.co.za/badger-spf34-sunscreen-anti-bug-balm-for-face-body?sfdr_ptcid=9581_617_522574210&sfdr_hash=95b024394b5d95642bfe4dd6e64867bd&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx8oeHwdtUYNs_I2Yg1ZhSQqi8G50v98yQgEQ66fwbECsQelnVpNka8aAqLvEALw_wcB [Accessed 22/03/ 2020].

Faithful to Nature. 2020d. *Biogrow bioneem, biogrow* [Online]. Available: https://www.faithful-to-nature.co.za/biogrow-bioneem?smplid=23558&sfdr_ptcid=9581_617_81050250&sfdr_hash=24a85d26ac489116e5aa5faf7c940781&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx_K5RGW048pUa8YVe2dWKWgLiHJb8w61q_E6cwdoy9jtE1dyzjIsIEaAm6AEALw_wcB#250=2803 [Accessed 21/03/ 2020].

Faithful to Nature. 2020e. *Biogrow vegol organic insecticide biogrow* [Online]. Available: https://www.faithful-to-nature.co.za/biogrow-vegol-organic-insecticide?sfdr_ptcid=9581_617_81049029&sfdr_hash=671102addddc171b2fe3ca392066db89&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx-

5Q_FmLrDSA53yGrf30hXT33PgUjAqxpv3WQ76CXrYQU6MSeI0PWYaAsYPEALw_wcB [Accessed 22/03/ 2020].

Faithful to Nature. 2020f. *Earthsap bugs away roll-on, earthsap* [Online]. Available: https://www.faithful-to-nature.co.za/earthsap-bugs-away-roll-on?sfdr_ptcid=9581_617_81050772&sfdr_hash=10a131f9bb05a335dc42654cd37c16b3&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx-fW5ZlUdTYU70iC56mWGCyYIvDY3zBupI8WbrcYBCFU3P4WJZXKmMaAoz1EALw_wcB [Accessed 22/03/ 2020].

Faithful to Nature. 2020h. *Kiddiekix little explorer bugz off insect repellent kiddiekix* [Online]. Available: https://www.faithful-to-nature.co.za/kiddiekix-little-explorer-bugz-off-insect-repellent?sfdr_ptcid=9581_617_81051117&sfdr_hash=64b442aba9c4878e099c975c296a9601&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx_eaHPyiCLG8jZjRAuHeT7RGFUNVxudSWe3sW1964TmRo1nBjUZgz4aAhpxEALw_wcB [Accessed 22/03/ 2020].

Faithful to Nature. 2020i. *Natural orange house hold insect repellent natural orange* [Online]. Available: https://www.faithful-to-nature.co.za/natural-orange-house-hold-insect-repellent?li_source=LI&li_medium=related-products&li_pl=63706326-9dac-4833-8db0-6859c079860e&li_tr=related-products [Accessed 21/03/ 2020].

Faithful to Nature. 2020j. *Oh-lief natural olive insect repellent balm, oh-lief natural olive skincare* [Online]. Available: https://www.faithful-to-nature.co.za/oh-lief-natural-olive-insect-repellent-balm?smplid=66803&sfdr_ptcid=9581_617_422447540&sfdr_hash=6fbf9b8cff25b979316d6fdb2ad9545b&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx8cWoM5xDctRlZ9_4cWpyPnit7qQ5zl8I69LlxnbGqfU5Zcv8-R9LEaAiV8EALw_wcB#250=2849 [Accessed 21/03/ 2020].

Faithful to Nature. 2020k. *Pannatural pets anti-bug spray, pannatural pets* [Online]. Available: https://www.faithful-to-nature.co.za/natura-pets-insect-repellent-spray?sfdr_ptcid=9581_617_272293605&sfdr_hash=ef95dd44b0b8e18a4dce0853674746b1&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx8Z91kQ_-Pqq2MTaIG-GbkZdODL16S9zo3Q-mePPmzuOW1DitUm0z4aAitPEALw_wcB [Accessed 21/03/ 2020].

Faithful to Nature. 2020l. *Soylites coconut candle - clear jar - insect repellent blend, soylites* [Online]. Available: https://www.faithful-to-nature.co.za/soylites-coconut-candle-clear-jar-insect-repellent-blend?sfdr_ptcid=9581_617_272292828&sfdr_hash=97088c2ee108ccfe0c71fcea14fb9ea6&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx8kgptf3_idoPBwp0VAGUTpNAkYOy_nqaSb4GxRVO1zu1WvdMKTn3kaAssAEALw_wcB [Accessed 21/03/ 2020].

FaithfultoNature. 2020g. *Just pure natural insect repellent just pure* [Online]. Available: https://www.faithful-to-nature.co.za/just-pure-natural-insect-repellent?sfdr_ptcid=9581_617_81063054&sfdr_hash=7289319fea3809e24b2d3cd81c74d20e&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx9tK7mHcnwYQYaMIMP9Q0N7agPcbHARSGwBU2yS4X2dKFj7OPPt2YgaAkkrEALw_wcB [Accessed 21/03/ 2020].

FAWCO. 2021. *Literacy in nigeria (sdg target 4.6)* [Online]. Available: https://www.fawco.org/global-issues/education/education-articles/4623-literacy-in-nigeria-sdg-target-4-6 [Accessed 16/01/ 2022].

Feng, H.-m. 2001. *Switchable mosquito expelling/killing device* [Online]. Google Patents. Available: https://patents.google.com/patent/US6293044B1/en [Accessed 15/04/ 2020].

Feuser, Z. P., Colonetti, T., Grande, A. J., Uggioni, M. L. R., Roever, L. & Da Rosa, M. I. 2020. Efficacy of the DEET, IR3535, and Picaridin Topical Use Against *Aedes aegypti*: Systematic Review. *Infectious Diseases In Clinical Practice,* 28**,** 327-341.

FirstNature. 2011. *Samuel frederick gray (1766 - 1828) - a brief biography* [Online]. Available: https://www.first-nature.com/fungi/~biog-gray.php [Accessed 22/01/ 2020].

FMOH. 2005. *National antimalarial treatment policy* [Online]. Available: http://digicollection.org/hss/documents/s18401en/s18401en.pdf [Accessed 02/11/ 2021].

FMOH. 2009. *Malaria operational plan in nigeria (mop)* [Online]. Available: https://www.google.com/search?client=firefox-b-d&q=Malaria+oprational+plan+2013 [Accessed 12/01/ 2022].

FMOH. 2013. *Malaria-lymphatic filariasis co-implementation in nigeria* [Online]. Available: https://www.health.gov.ng/doc/guidelines-malaria-lf-co-implementation-nigeria-.pdf [Accessed 26/10/2021 2021].

FMOH. 2014. *National malaria strategic plan 2014 – 2020* [Online]. Available: https://www.health.gov.ng/doc/NMEP-Strategic-Plan.pdf [Accessed 06/02/ 2021].

Forero, D. A., Chaparro, P. E., Vallejo, A. F., Benavides, Y., Gutiérrez, J. B., Arévalo-Herrera, M., et al. 2014. Knowledge, attitudes and practices of malaria in Colombia. *Malaria Journal,* 13**,** 165-174.

Fradin, M. S. & Day, J. F. 2002. Comparative efficacy of insect repellents against mosquito bites. *New England Journal of Medicine,* 347**,** 13-18.

Fu, H.-G., Li, Z.-W., Hu, X.-X., Si, S.-Y., You, X.-F., Tang, S., et al. 2019. Synthesis and biological evaluation of quinoline derivatives as a novel class of broad-spectrum antibacterial agents. *Molecules,* 24**,** 548-559.

Fuge, T. G., Ayanto, S. Y. & Gurmamo, F. L. 2015. Assessment of knowledge, attitude and practice about malaria and itns utilization among pregnant women in shashogo District, Southern Ethiopia. *Malaria Journal,* 14**,** 235-243.

Future Light. 2019. *Led mosquito repellent globe* [Online]. Available: https://www.futurelight.co.za/products/led-mosquito-repellent-globe?variant=18682331299898&sfdr_ptcid=2682_617_360773583&sfdr_hash=23be917fcdb677760a718ebd2a314696&gclid=Cj0KCQiA0ZHwBRCRARIsAK0Tr-osTFsT6idVHX9W_RdWAnx4pIrSjHKJ0gkXfhwz8W13NKvNkHSTvAUaAkflEALw_wcB [Accessed 26/12/ 2019].

Gaillard, T., Madamet, M., Tsombeng, F. F., Dormoi, J. & Pradines, B. 2016. Antibiotics in malaria therapy: Which antibiotics except tetracyclines and macrolides may be used against malaria? *Malaria Journal,* 15**,** 556-565.

Game. 2020a. *Efekto - 100ml mole repellent* [Online]. Available: https://www.game.co.za/game-za/en/All-Game-Categories/Home-%26-Garden/Garden-Care/Insecticides/100ML-MOLE-REPELLENT/p/00669085 [Accessed 26/04/ 2020].

Game. 2020b. *Homemark - pest magic ultrasonic insect repeller* [Online]. Available: https://www.game.co.za/game-za/en/All-Game-Categories/DIY-%26-Auto/Lighting/Torches-%26-Emergency-Lights/Pest-Magic-Ultrasonic-Insect-Repeller/p/00449198?gclid=CjwKCAjw4pT1BRBUEiwAm5QuRw7jdPvCU50gpWYgKzbVGYgEtzWHCUBsIx5r8Ck5xmkaxaRCw5FmiBoCJ5gQAvD_BwE [Accessed 26/04/ 2020].

Game. 2020c. *Leisure quip - usb rechargeable mosquito killer with led light* [Online]. Available: https://www.game.co.za/game-za/en/All-Game-Categories/DIY-%26-Auto/Lighting/Torches-%26-Emergency-Lights/USB-RECHARGEABLE-MOSQUITO-KILLER-WITH-LED-LIGHT/p/00786610 [Accessed 26/04/ 2020].

Game. 2020d. *Rep.Umbrella - citronella oil 1.5l* [Online]. Available: https://www.game.co.za/game-za/en/All-Game-Categories/Sports-%26-Leisure/Camping-%26-Hiking/Camping-Accessories/CITRONELLA-OIL-1-5L/p/00565368 [Accessed 26/04/ 2020].

Gearbest. 2014. *Non-toxic uv mosquito killer lamp insect trap - white* [Online]. Available: https://www.gearbest.com/other-garden-supplies/pp_009641139474.html?wid=1433363&currency=ZAR&vip=2373337&gclid=CjwKCAiAuqHwBRAQEiwAD-zr3e0KT0qPI0RFnSekeaAjDFivnD6GjTcfbdq5CktziGFhhH467iwigBoC22YQAvD_BwE [Accessed 29/12/ 2019].

Ghouth, A. S. B. 2013. Availability and prescription practice of anti-malaria drugs in the private health sector in Yemen. *The Journal of Infection in Developing Countries,* 7**,** 404-412.

Gillies, M. & Coetzee, M. 1987. A supplement to the Anophelinae of Africa south of the sahara. Gillies, M. & Coetzee, M. 1987. A supplement to the Anophelinae of Africa South of the Sahara. *Publications Of The. South African Institute For Medical Research,* 55**,** 1-143.

Gillies, M. T. & De Meillon, B. 1968. The Anophelinae of Africa south of the Sahara (Ethiopian zoogeographical region). *The Anophelinae Of Africa South Of The Sahara (Ethiopian Zoogeographical Region).* 55**,** 1-145.

Gilson, P. R., Nguyen, W., Poole, W. A., Teixeira, J. E., Thompson, J. K., Guo, K., et al. 2019. Evaluation of 4-Amino 2-Anilinoquinazolines against *Plasmodium* and Other Apicomplexan Parasites In Vitro and in a *P. falciparum* Humanized NOD-scid IL2Rgamma(null) Mouse Model of Malaria. *Antimicrobial Agents and Chemotherapy,* 63**,** 1-14.

Goel, P. & Gerriets, V. 2019. *Chloroquine* [Online]. StatPearls Publishing. Available: https://europepmc.org/article/NBK/nbk551512 [Accessed 04/03/ 2020].

Goodyer, L. & Schofield, S. 2018. Mosquito repellents for the traveller: Does picaridin provide longer protection than DEET? *Journal of travel medicine,* 25**,** S10-S15.

Goodyer, L. 2019. *Advising patients about malaria risks and prevention* [Online]. Available: https://www.pharmaceutical-journal.com/learning/learning-article/advising-patients-about-malaria-risks-and-prevention/20206208.article?firstPass=false [Accessed 19/04/ 2020].

Googlemap. 2022a. *Google Map location of Charlotte Maxeke Johannesburg Academic Hospital* [Online]. Available: https://www.google.com/search?q=google+map+location+of+charlotte+maxeke+hospital&tbm=isch&ved=2ahUKEwiuqL-g95X2AhUWxeAKHWEBDHkQ2-cCegQIABAA&oq=google+map+location+of+charlotte+maxeke+hospital&gs_lcp=CgNpbWcQAzoHCCMQ7wMQJ1CfCFiMSGDBTGgAcAB4AIAB0gOIAfMXkgEHMi0zLjQuMpgBAKABAaoBC2d3cy13aXotaW1nwAEB&sclient=img&ei=sTYWYu6LJpaKgwfhgrDIBw&client=firefox-b-d#imgrc=wT5yEAaQDC-4kM [Accessed 8/04/ 2022].

Googlemap. 2022b. *Google map location of Chris-Hani Baragwanath Hospital* [Online]. Available: https://www.google.com/search?q=google+map+location+of+chris+hani&tbm=isch&ved=2ahUKEwjT99O57v72AhUZgv0HHcddBJ8Q2-cCegQIABAA&oq=google+map+location+of+chris+hani&gs_lcp=CgNpbWcQAzoHCCMQ7wMQJ1DtCFjsPmCuR2gAcAB4AIABsgKIAZQ1kgEGMi0yNi4xmAEAoAEBqgELZ3dzLXdpei1pbWfAAQE&sclient=img&ei=UzpNYpMCmYT27w_Hu5H4CQ&client=firefox-b-d#imgrc=ATsdjvfBw48p-M [Accessed 08/04 2022].

Googlemap. 2022c. *Google Map Location of Federal Medical Centre Birnin Kebbi* [Online]. Available: https://www.google.com/search?q=GOOGLE+MAP+LOCATION+OF+FMC+BIRNIN+KEBBI&tbm=isch&ved=2ahUKEwi50dSVjJb2AhUCCXcKHQ6XAZAQ2-cCegQIABAA&oq=GOOGLE+MAP+LOCATION+OF+FMC+BIRNIN+KEBBI&gs_lcp=CgNpbWcQAzoHCCMQ7wMQJzoFCAAQgAQ6BAgAEEM6CAgAELEDEIMBOggIABCABBCxAzoHCAAQsQMQQzoGCAAQCBAeOgQIABAYUOUPWJyNAWDJkQFoAHAAeACAAf0CiAHCXJIBBzItMjQuMTaYAQCgAQGqAQtnd3Mtd2l6LWltZ8ABAQ&sclient=img&ei=oEwWYrmBA4KS3AOOroaACQ&bih=643&biw=1349&client=firefox-b-d&hl=en#imgrc=mrfg04RrODPHPM [Accessed 11/04/ 2022].

Googlemap. 2022d. *Google map location of Helen Joseph Hospital in Johannesburg* [Online]. Available: https://www.google.com/search?q=google+map+location+of+charlotte+maxeke+h

ospital&tbm=isch&ved=2ahUKEwiuqL-g95X2AhUWxeAKHWEBDHkQ2-cCegQIABAA&oq=google+map+location+of+charlotte+maxeke+hospital&gs_lcp=CgNpbWcQAzoHCCMQ7wMQJ1CfCFiMSGDBTGgAcAB4AIAB0gOIAfMXkgEHMi0zLjQuMpgBAKABAaoBC2d3cy13aXotaW1nwAEB&sclient=img&ei=sTYWYu6LJpaKgwfhgrDIBw&client=firefox-b-d#imgrc=wT5yEAaQDC-4kM [Accessed 11/04/ 2022].

Googlemap. 2022e. *Google Map Location of Sir Yahaya Memorial Hospital* [Online]. Available: https://www.google.com/search?q=GOOGLE+MAP+LOCATION+OF+SIR+YAHYA+MEMORIAL+HOSPITAL+BIRNIN+KEBBI&tbm=isch&ved=2ahUKEwjsp4qijJb2AhUE2eAKHYDgAy8Q2-cCegQIABAA&oq=GOOGLE+MAP+LOCATION+OF+SIR+YAHYA+MEMORIAL+HOSPITAL+BIRNIN+KEBBI&gs_lcp=CgNpbWcQA1CzEljxdmC6emgAcAB4AIABuAOIAbI8kgEIMi0yMy40LjGYAQCgAQGqAQtnd3Mtd2l6LWltZ8ABAQ&sclient=img&ei=ukwWYuziBYSygweAwY_4Ag&bih=643&biw=1349&client=firefox-b-d&hl=en#imgrc=fppdWd5ZA_z_ZM [Accessed 11/04/ 2022].

Govere, J., Durrheim, D. N., Baker, L., Hunt, R. & Coetzee, M. 2000b. Efficacy of three insect repellents against the malaria vector *Anopheles arabiensi*s. M*edical and Veterinary Entomology*, 14, 441-444.

Govere, J., Durrheim, D., la Grange, K., Mabuza, A. & Booman, M. 2000a. Community knowledge and perceptions about malaria and practices influencing malaria control in Mpumalanga Province, South Africa. *South African medical journal,* 90**,** 611-618.

Greener Ways Organic. 2020. *Greenerways organic mosquito repellent zone - new improved formula, natural backyard insect repellent outdoor mosquito repellant pest control, deet-free (3 pack)* [Online]. Available: https://www.ubuy.za.com/search/index/view/product/B07VXLTXJX/s/greenerways-organic-mosquito-repellent-zone-new-improved-formula-natural-backyard-insect-repellent-outdoor-mosquito-repellant-pest-control-deet-free-3-pack/store/store/kk/dp?ref_p=dp-rp [Accessed 26/04/ 2020].

Gruenberg, M., Hofmann, N. E., Nate, E., Karl, S., Robinson, L. J., Lanke, K., et al. 2019. qRT-PCR versus IFA-based Quantification of Male and Female Gametocytes in Low-Density *Plasmodium falciparum* Infections and Their Relevance for Transmission. *The Journal Of Infectious Diseases,* 221**,** 598–607.

Guardian. 2014. *Nigeria's president signs law imposing up to 14 years' jail for gay relationships* [Online]. Available: https://www.theguardian.com/world/2014/jan/13/nigerian-president-signs-anti-gay-law [Accessed 15/04/ 2022].

Guest, C., Pinder, M., Doggett, M., Squires, C., Affara, M., Kandeh, B., et al. 2019. Trained dogs identify people with malaria parasites by their odour. *The Lancet Infectious Diseases,* 19**,** 578-580.

Gulen, M. & Satar, S. 2020. Uncommon presentation of covid-19: Gastrointestinal bleeding. *Clinics and Research in Hepatology and Gastroenterology,* 44**,** e72-e76.

Gupta, P. 2017. *Design synthesis and characterization of some novel compounds for insect repellency screening* [Online]. Available: http://ir.inflibnet.ac.in:8080/jspui/bitstream/10603/185934/5/05_introduction.pdf [Accessed 16/01/ 2020].

Haanshuus, C. G., Mørch, K., Blomberg, B., Strøm, G. E. A., Langeland, N., Hanevik, K., et al. 2019. Assessment of malaria real-time PCR methods and application with focus on low-level parasitaemia. *Plos One,* 14**,** e0218982-e0218987.

Habimana, A., Harerimana, A., Asingizwe, D., Nyandwi, T. & Njunwa, K. J. 2016. Community health workers' knowledge, attitudes and practices about malaria prevention in Gicumbi District, Rwanda. *Rwanda Journal,* 3**,** 27-35.

Haldar, K., Bhattacharjee, S. & Safeukui, I. 2018. Drug resistance in *Plasmodium*. *Nature Reviews Microbiology,* 16**,** 156-170.

Hanem Fathy Khater, Abdelfattah M. Selim, Galal A. Abouelella, Nour A. Abouelella, Kadarkarai Murugan & Govindarajan, N. P. V. a. M. 2019. *Commercial mosquito repellents and their safety concerns* [Online]. Available: https://www.intechopen.com/online-first/commercial-mosquito-repellents-and-their-safety-concerns [Accessed 3/11/ 2019].

Harismah, K., Vitasari, D., Mirzaei, M., Fuadi, A. M. & Aryanto, Y. H. 2017. Protection capacity of mosquito repellent ink from citronella (*Cymbopogon nardus* l.) and clove leaf oils (*Syzygium aromaticum*) againts *Aedes aegypti*. *AIP Conference Proceedings,* 1855**,** 020023_1-20023_6.

Hastings, I. M., Hodel, E. M. & Kay, K. 2016. Quantifying the pharmacology of antimalarial drug combination therapy. *Scientific Reports,* 6**,** 32762-3279.

Heller, L. E. & Roepe, P. D. 2019. Artemisinin-based antimalarial drug therapy: Molecular pharmacology and evolving resistance. *Tropical Medicine and Infectious Disease,* 4**,** 89-95.

Herchline, T. E. & Simon, R. Q. 2019. *Malaria medication* [Online]. Available: https://emedicine.medscape.com/article/221134-medication [Accessed 2/11/ 2019].

Hlongwana, K. W., Mavundza, E. J., Mohapi, E. P., Kruger, P., Urbach, J., Mukaratirwa, S., et al. 2013. Vector-control personnel's knowledge, perceptions and practices towards insecticides used for indoor residual spraying in Limpopo Province, South Africa. *Parasites & Vectors,* 6**,** 118-127.

Ho, K.-C., Mo, S.-Y. & Tang, B.-B. 2019. Comparing mosquito repellency efficacy on textiles sprayed with DEET and permethrin. *Chemical and Pharmaceutical Research,* 1**,** 1-4.

Hospital, H. J. 2021. *Helen Joseph Hospital* [Online]. Available: https://en.wikipedia.org/wiki/Helen_Joseph_Hospital [Accessed 5/02/ 2022].

Hospital, T. C. H. B. 2010. *Chris Hani Baragwanath Hospital the world's 3rd biggest hospital, in South Africa.* [Online]. Available: https://www.chrishanibaragwanathhospital.co.za/ [Accessed 25/03/ 2019].

Huang, L., Mwebaza, N., Kajubi, R., Marzan, F., Forsman, C., Parikh, S., et al. 2018. Strong correlation of lumefantrine concentrations in capillary and venous plasma from malaria patients. *Public Library Of Science One,* 13**,** e0202082-e0202092.

Huang, L., Parikh, S., Rosenthal, P. J., Lizak, P., Marzan, F., Dorsey, G., et al. 2012. Concomitant efavirenz reduces pharmacokinetic exposure to the antimalarial drug artemether-lumefantrine in healthy volunteers. *Journal Of Acquired Immune Deficiency Syndromes (1999),* 61**,** 310-316.

Humandignitytrust. 2022. *LGBTI in Nigeria.* [Online]. Available: https://www.humandignitytrust.org/country-profile/nigeria/ [Accessed 15/04/ 2022].

InfoNamibia. 2020. *Namibias geography* [Online]. Available: https://www.info-namibia.com/info/namibias-geography [Accessed 26/05/ 2020].

Islam, J., Zaman, K., Duarah, S., Raju, P. S. & Chattopadhyay, P. 2017a. Mosquito repellents: An insight into the chronological perspectives and novel discoveries. *Acta Tropica,* 167**,** 216-230.

Islam, J., Zaman, K., Tyagi, V., Duarah, S., Dhiman, S. & Chattopadhyay, P. 2017b. Protection against mosquito vectors *Aedes aegypti, Anopheles stephensi* and *Culex quinquefasciatus* using a novel insect repellent, ethyl anthranilate. *Acta Tropica,* 174**,** 56-63.

Ismail, A. & Oke, I. 2012. Trend analysis of precipitation in Birnin Kebbi, Nigeria. *International Research Journal of Agricultural Science and Soil Science,* 2**,** 286-297.

Ita, O. I., Otu, A. A., Onyedibe, K., Iwuafor, A. A., Banwat, E. & Egah, D. Z. 2018. A diagnostic performance evaluation of rapid diagnostic tests and microscopy for malaria diagnosis using nested polymerase chain reaction as reference standard in a tertiary hospital in Jos, Nigeria. *Transactions of The Royal Society of Tropical Medicine and Hygiene,* 112**,** 436-442.

Ivanescu, B., Miron, A. & Corciova, A. 2015. Sesquiterpene lactones from artemisia genus: Biological activities and methods of analysis. *Journal of Analytical Methods in Chemistry,* 2015**,** 21-42.

Iyigundogdu, Z., Kalayci, S., Asutay, A. B. & Sahin, F. 2019. Determination of antimicrobial and antiviral properties of IR3535. *Molecular Biology Reports,* 46**,** 1819-1824.

Jacob, V. & Nuuyoma, V. 2019. Knowledge, attitudes and practices of the university students on malaria prevention in Kavango East, Namibia. *Global Journal of Health Science,* 11**,** 102-109.

Jan, Z., Khan, A., Sajjad, M., Muhammad, K., Rho, S. & Mehmood, I. 2018. A review on automated diagnosis of malaria parasite in microscopic blood smears images. *Multimedia Tools and Applications,* 77**,** 9801-9826.

Jauréguiberry, S. 2019. [severe and complicated malaria]. *La Revue du praticien,* 69**,** 162-165.

Kadam, S., Adhav, A., Mote, B., Kalaskar, S., Thirumugam, M., Kurbude, R., et al. 2015. Knowledge, attitude, and practices of people towards malaria in tribal communities of Jawhar, Maharashtra, India. *International Journal Of Current Research And Review,* 7**,** 25-31.

Kajubi, R., Ochieng, T., Kakuru, A., Jagannathan, P., Nakalembe, M., Ruel, T., et al. 2019. Monthly sulfadoxine–pyrimethamine versus dihydroartemisinin–piperaquine

for intermittent preventive treatment of malaria in pregnancy : a double-blind, randomised, controlled, superiority trial. *The Lancet,* 393**,** 1428-1439.

Kalilani-Phiri, L. V., Lungu, D. & Coghlan, R. 2011. Knowledge and malaria treatment practices using artemisinin combination therapy (ACT) in Malawi: Survey of health professionals. *Malaria Journal,* 10**,** 279-285.

Kamal-Yanni, M. M., Potet, J. & Saunders, P. M. 2012. Scaling-up malaria treatment: A review of the performance of different providers. *Malaria Journal,* 11**,** 414-423.

Kamatou, G. P.; Van Zyl, R. L.; Davids, H.; Van Heerden, F. R.; Lourens, A. C.; Viljoen, A. M. 2008. Antimalarial and anticancer activities of selected South African Salvia species and isolated compounds from *S. radula*. *South African Journal Of Botany*, 7, 238-243.

Karunajeewa, H. & Berman, J. 2019. Is the Epidemiology of *Plasmodium knowlesi* Changing, and What Does This Mean for Malaria Control in Southeast Asia? *Clinical Infectious Diseases,* 70, 368–369.

Kasstan, B., Hampshire, K., Guest, C., Logan, J. G., Pinder, M., Williams, K., et al. 2019. Sniff and tell: the feasibility of using bio-detection dogs as a mobile diagnostic intervention for asymptomatic malaria in Sub-Saharan Africa. *Journal Of Biosocial Science,* 51**,** 436-443.

Katzung Bertram G & Rosenthal, P. J. 2004. Antiprotozoal Drugs. 13 ed. New York Chicago: Mc Grow Hill Education.

KeaneCreative. 1997. *Perceptions and attitudes* [Online]. Available: https://keanecreative.co.uk/blog/article/perceptions-and-attitudes [Accessed 28/05 2020].

Kebbi, F. B. 2022. *Federal Medical Centre Birnin Kebbi* [Online]. Available: https://fmcbirninkebbi.gov.ng/home/about_us [Accessed 05/02/ 2022].

Kebede, D., Hibstu, D., Birhanu, B. & Bekele, F. 2017. Knowledge, attitude and practice towards malaria and associated factors in Areka Town, Southern Ethiopia: Community-based cross sectional study. *Journal of Tropical Diseases,* 5**,** 1-11.

Kelly, M., Su, C.-Y., Schaber, C., Crowley, J. R., Hsu, F.-F., Carlson, J. R., et al. 2015. Malaria Parasites Produce Volatile Mosquito Attractants. *Microbiology,* 6**,** e00235-e00240.

Khater, H. F. 2017. Introductory chapter: Back to the future-solutions for parasitic problems as old as the pyramids. *Natural Remedies in the Fight against Parasites*, 5-7.

Khater, H. F., Selim, A. M., Abouelella, G. A., Abouelella, N. A., Murugan, K., Vaz, N. P., et al. 2019. *Commercial mosquito repellents and their safety concerns* [Online]. IntechOpen. Available: https://www.intechopen.com/chapters/68538 [Accessed 15/04/ 2019].

Khera, A. & Mukherjee, R. 2019. Artemisinin resistance: Cause for worry? *Journal of Marine Medical Society,* 21**,** 4-8.

Killeen, G. F. 2014. Characterizing, controlling and eliminating residual malaria transmission. *Malaria Journal,* 13**,** 330-352.

Kim, H. K., Seo, J.-W. & Kim, G.-H. 2020. Various effects of volatile constituents from magnolia kobus flowers against *Aedes albopictus* (diptera: Culicidae). *Industrial Crops and Products,* 145**,** 112109-112114.

Kinung'hi, S. M., Mashauri, F., Mwanga, J. R., Nnko, S. E., Kaatano, G. M., Malima, R., et al. 2010. Knowledge, attitudes and practices about malaria among communities: Comparing epidemic and non-epidemic prone communities of Muleba district, North-western Tanzania. *BioMed Central Public Health,* 10**,** 395-406.

Klicks+. 2020a. *Doom destroyer mosquito room spray 180ml* [Online]. Available: https://clicks.co.za/doom_destroyer-mosquito-room-spray-180ml/p/101754 [Accessed 24/04/ 2020].

Klicks+. 2020b. *Mortein multi insect killer low odour 300ml* [Online]. Available: https://clicks.co.za/mortein_multi-insect-killer-low-odour-300ml/p/699363 [Accessed 24/04/ 2020].

Klicks+. 2020c. *Mortein naturgard insect control system* [Online]. Available: https://clicks.co.za/mortein_naturgard-insect-control-system/p/237996 [Accessed 24/04/ 2020].

Klicks+. 2020d. *Peaceful sleep mosquito room spray* [Online]. Available: https://clicks.co.za/peaceful-sleep_mosquito-room-spray/p/250471 [Accessed 24/04/ 2020].

Klicks+. 2020e. *Raid electric diffuser* [Online]. Available: https://clicks.co.za/raid_electric-diffuser/p/123324 [Accessed 24/04/ 2020].

Klicks+. 2020f. *Tabard citronella night lights 18's* [Online]. Available: https://clicks.co.za/tabard_citronella-night-lights-18s/p/254719 [Accessed 24/04/ 2020].

Kloprogge, F., Workman, L., Borrmann, S., Tékété, M., Lefèvre, G., Hamed, K., et al. 2018. Artemether-lumefantrine dosing for malaria treatment in young children and pregnant women: A pharmacokinetic-pharmacodynamic meta-analysis. *Public Library Of Science Medicine,* 15**,** e1002579-e1002604.

Koekemoer, L. L., Spillings, B. L., Christian, R. N., Lo, T.-C. M., Kaiser, M. L., Norton, R. A., et al. 2011. Multiple insecticide resistance in *Anopheles gambiae* (Diptera: Culicidae) from pointe Noire, Republic of the Congo. *Vector-Borne And Zoonotic Diseases,* 11**,** 1193-1200.

Koenker, H., Arnold, F., Ba, F., Cisse, M., Diouf, L., Eckert, E., et al. 2018. Assessing whether universal coverage with insecticide-treated nets has been achieved: is the right indicator being used? *Malaria Journal,* 17**,** 355-365.

Kouakou, Y. I., Tod, M., Leboucher, G., Lavoignat, A., Bonnot, G., Bienvenu, A.-L., et al. 2019. Systematic review of artesunate pharmacokinetics : Implication for treatment of resistant malaria. *International Journal Of Infectious Diseases,* 89**,** 30-44.

Kudyba, H. M., Louzada, J., Ljolje, D., Kudyba, K. A., Muralidharan, V., Oliveira-Ferreira, J., et al. 2019. Field evaluation of malaria malachite green loop-mediated isothermal amplification in health posts in Roraima state, Brazil. *Malaria Journal,* 18**,** 98-104.

Kulkarni, M. M., Jacob, G. P., Kamath, A., Guha, S. & Ramireddy, M. 2017. Knowledge, attitude, and practices regarding mosquito borne diseases among adults in Udupi District, Karnataka. *Indian Journal Of Forensic And Community Medicine,* 4**,** 158-163.

Laar, A., Laar, A. K. & Dalinjong, P. A. 2013. Community perception of malaria and its influence on health-seeking behaviour in rural ghana: A descriptive study. *Malaria World Journal,* 4**,** 269-278.

Labama Otuli, N., Marini Djang'eing'a, R., Losimba Likwela, J., Bosenge Nguma, J. D., Maindo Alongo, M. A., Ahuka Ona Longombe, A., et al. 2021. Efficacy and safety of malarial prophylaxis with mefloquine during pregnancy in Kisangani, Democratic

Republic of Congo: A randomized clinical trial. *British Journal Of Clinical Pharmacology,* 87**,** 3115-3126.

Ladi-Akinyemi, T. W., Amoran, O., Ogunyemi, A., Kanma-Okafor, O. & Onajole, A. 2018. Knowledge and implementation of the national malaria control programme among health-care workers in primary health-care centers in Ogun State, Nigeria. *Journal of Clinical Sciences,* 15**,** 48-54.

Lalremruata, A., Magris, M., Vivas-Martinez, S., Koehler, M., Esen, M., Kempaiah, P., et al. 2015. Natural infection of *Plasmodium brasilianum* in humans: Man, and monkey share quartan malaria parasites in the Venezuelan Amazon. *Ebiomedicine,* 2**,** 1186-1288.

Landman, K. Z., Tan, K. R. & Arguin, P. M. 2014. Knowledge, attitudes, and practices regarding antimalarial chemoprophylaxis in US Peace corps volunteers—Africa, 2013. *MMWR. Morbidity And Mortality Weekly Report,* 63**,** 516-517.

Laufer, M. K. 2019. Beyond birthweight: Benefits and risks of preventing malaria in pregnancy. *The Lancet,* 393**,** 1388-1390.

Lee, M. Y. 2018. Essential oils as repellents against arthropods. *BioMed Research International,* 2018**,** 6860271-6860281.

Legalaidsouthafrica. 2022. *Child rights based on age* [Online]. Available: https://legal-aid.co.za/2018/09/26/child-rights-based-on-age/ [Accessed 3/07/ 2022].

Legeay, S., Clere, N., Apaire-Marchais, V., Faure, S. & Lapied, B. 2018. Unusual modes of action of the repellent DEET in insects highlight some human side effects. *European Journal of Pharmacology,* 825**,** 92-98.

LEXICO. 2020. *Meaning of citronelle in English* [Online]. Available: https://www.lexico.com/definition/citronelle [Accessed 22/01/ 2020].

Li, S., Hu, L., Li, J., Zhu, J., Zeng, F., Huang, Q., Qiu, L., Du, R. & Cao, R. 2019. Design, synthesis, structure-activity relationships and mechanism of action of new quinoline derivatives as potential antitumor agents. *European Journal of Medicinal Chemistry,* 162**,** 666-678.

LightInTheBox.com. 2019. *New intelligent ultrasound artifact mosquito repellent bracelet ultrasonic pest repeller reject anti mosquito indoor outdoor* [Online]. Available: https://www.lightinthebox.com/en/p/new-intelligent-ultrasound-artifact-mosquito-repellent-bracelet-ultrasonic-pest-repeller-reject-anti-mosquito-indoor-

outdoor_p7423239.html?currency=ZAR&litb_from=paid_adwords_shopping&sku=1_36%7C444_27165&country_code=za&utm_source=google_shopping&utm_medium=cpc&adword_mt=&adword_ct=394646961249&adword_kw=&adword_pos=&adword_pl=&adword_net=u&adword_tar=&adw_src_id=4224179917_7913987690_81849239653_pla-656278395810&gclid=CjwKCAiAuqHwBRAQEiwAD-zr3fSW6L8kTObro8nUnqUbwPCdFZ39DhchdydL1P07dXro6_XzOWHRMhoCBtcQAvD_BwE [Accessed 29/12/ 2019].

Liu, J., Modrek, S., Gosling, R. D. & Feachem, R. G. 2013. Malaria eradication: Is it possible? Is it worth it? Should we do it? *The Lancet Global Health,* 1**,** e2-e3.

Lo, W. L., Mok, K. L. & Yu Pui Ming, S. D. 2018. Which insect repellents should we choose? Implications from results of local market survey and review of current guidelines. *Hong Kong Journal of Emergency Medicine,* 25**,** 272-280.

Loot.Co.Za. 2019. *Ugreen usb-powered mosquito repellent* [Online]. Available: https://www.loot.co.za/product/ugreen-usb-powered-mosquito-repellent/hjks-4959-g860?referrer=googlemerchant&referrer=google&PPC=Y&gclid=Cj0KCQiA0ZHwBRCRARIsAK0Tr-qgRK2nv8ZSwsM6HQEEgS5ehCoEAcNW9iay5qlqW8_wgYfX0ACKRz0aAnO9EALw_wcB&gclsrc=aw.ds [Accessed 26/12/ 2019].

Lula Ntamba, Y., Muhindo Mavoko, H., Kalabuanga, M., Fungula, B., Ntamabyaliro Nsengi, P.-M., Tona Lutete, G., et al. 2019. Safety and tolerability of artesunate-amodiaquine, artemether-lumefantrine and quinine plus clindamycin in the treatment of uncomplicated *Plasmodium falciparum* malaria in Kinshasa, the Democratic Republic of the Congo. *Public Library Of Science One,* 14**,** e0222379-e0222379.

Lupi, E., Hatz, C. & Schlagenhauf, P. 2013. The efficacy of repellents against *Aedes, Anopheles, Culex* and *Ixodes* spp. – a literature review. *Travel medicine and infectious disease,* 11**,** 374–411.

Ma, Y., Li, M., Zhang, H., Sun, H., Su, H., Wang, Y. & Du, Z. 2019. Bioassay-guided isolation of active compounds from adenosma buchneroides essential oil as mosquito repellent against *Aedes albopictu*s. *Journal of Ethnopharmacology,* 231**,** 386-393.

Maduka, O. 2018. End malaria for good: a review of current strategies and future novelties for malaria elimination in Nigeria. *Microwave Journal,* 9**,** 1-4.

Maharaj, R., Seocharan, I., Qwabe, B., Mkhabela, M., Kissoon, S. & Lakan, V. 2019. Decadal epidemiology of malaria in Kwazulu-Natal, a province in South Africa targeting elimination. *Malaria journal,* 18**,** 368-374.

Maia, M. F. & Moore, S. J. 2011. Plant-based insect repellents: A review of their efficacy, development and testing. *Malaria Journal,* 10**,** S11-S25.

Makhubu, N. 2016. *City has most literate adults in country* [Online]. Available: https://www.iol.co.za/capetimes/news/city-has-most-literate-adults-in-country-2029816 [Accessed 01/05/ 2020].

Makro. 2019. *Sothing cactus mosquito killer and repellent electric usb uv light* [Online]. Available: https://www.makro.co.za/sports-outdoor-travel/camping/camping-accessories/camping-accessories/sothing-cactus-mosquito-killer-and-repellent-electric-usb-uv-light/p/c77a60f0-9aa7-4caa-ba25-fd212f5156a4?gclid=Cj0KCQiA0ZHwBRCRARIsAK0Tr-qA8nILljmGArgimWgNNDkqpHI4RKL7ccovCUxEL8w5DHBgztdnfj0aAhe2EALw_wcB [Accessed 26/12/ 2019].

MalariaSite. 2016. *Malaria in wars and victims* [Online]. Available: https://www.malariasite.com/wars-victims/ [Accessed 15/11/ 2019].

Manana, P. N., Kuonza, L., Musekiwa, A., Mpangane, H. D. & Koekemoer, L. L. 2017. Knowledge, attitudes and practices on malaria transmission in Mamfene, KwaZulu-Natal Province, South Africa 2015. *Biomed Central Public Health,* 18**,** 41-47.

Manana, P. N., Kuonza, L., Musekiwa, A., Mpangane, H. D. & Koekemoer, L. L. 2018. Knowledge, attitudes and practices on malaria transmission in Mamfene, Kwazulu-Natal Province, South Africa 2015. *Biomed Central Public Health,* 18**,** 41-47.

Mannan, A. A., Elmardi, K. A., Idris, Y. A., Spector, J. M., Ali, N. A. & Malik, E. M. 2015. Do frontline health care providers know enough about artemisinin–based combination therapy to rationally treat malaria? A cross-sectional survey in Gezira State, Sudan. *Malaria Journal,* 14**,** 131-137.

Manohar, M., Muthukrishnan, G., Jebamony, K. & Radhakrishnan, S. 2017. Awareness and treatment seeking behaviour of malaria in selected endemic and non-endemic rural areas of Kanyakumari District, Tamil Nadu, India. *International Journal of Community Medicine And Public Health,* 3**,** 2313-8.

Marsh, A., Hirve, S., Lele, P., Chavan, U., Bhattacharjee, T., Nair, H., et al. 2020. Determinants and patterns of care-seeking for childhood illness in rural Pune District, India. *Journal Of Global Health,* 10**,** 1-13.

Martinez, P. D. G., Krake, S. H., Poggi, M. L., Campbell, S. F., Willis, P. A. & Dias, L. C. 2018. 2,3,8-trisubstituted quinolines with antimalarial activity. *Anais Da Academia Brasileira De Ciências,* 90**,** 1215-1231.

Mathiba, R. M., Mathivha, L. R. & Nethathe, G. D. 2019. Artesunate compared with quinine for the treatment of severe malaria in adult patients managed in an intensive care unit: A retrospective observational study. *Southern African Journal Of Critical Care (Online),* 35**,** 8-13.

Maverickcitizen. 2021. *South Africa's literacy rates plunge deeper as learning time is lost* [Online]. Available: https://www.dailymaverick.co.za/article/2021-09-13-south-africas-literacy-rates-plunge-deeper-as-learning-time-is-lost/ [Accessed 16/01/ 2022].

Mazigo, H. D., Obasy, E., Mauka, W., Manyiri, P., Zinga, M., Kweka, E. J., et al. 2010. Knowledge, Attitudes, and Practices about Malaria and Its Control in Rural Northwest Tanzania. *Malaria Research And Treatment,* 2010**,** 794261-794269.

Mbakilwa, H., Manga, C., Kibona, S., Mtei, F., Meta, J., Shoo, A., et al. 2012. Quality of malaria microscopy in 12 district hospital laboratories in Tanzania. *Pathogens And Global Health,* 106**,** 330-334.

Mehta, D., Solanki, H., Patel, P., Umat, P., Chauhan, R., Shukla, S., et al. 2015. A study on knowledge, attitude & practice regarding mosquito borne diseases in an urban area of Bhavnagar. *Health,* 6**,** 29-32.

Mehta, D., Solanki, H., Patel, P., Umat, P., Chauhan, R., Shukla, S., et al. 2015. A study on knowledge, attitude & practice regarding mosquito borne diseases in an urban area of Bhavnagar. *Healthline Journal,* 6**,** 29-32.

Meltzer, E. & Schwartz, E. 2019. Atovaquone-proguanil chemoprophylaxis in the era of tafenoquine. *Journal Of Travel Medicine,* 26**,** 133-135.

Menger, D. J., Otieno, B., de Rijk, M., Mukabana, W. R., van Loon, J. J. & Takken, W. 2014. A push-pull system to reduce house entry of malaria mosquitoes. *Malaria Journal,* 13**,** 1-8.

MERCK. 2019. *Discover everything about our insect repellent IR3535®* [Online]. Available: https://www.merckgroup.com/en/expertise/cosmetics/care-solutions/insect-repellent/about-IR3535.html [Accessed 9/01/ 2020].

Mfuh, K. O., Achonduh-Atijegbe, O. A., Bekindaka, O. N., Esemu, L. F., Mbakop, C. D., Gandhi, K., et al. 2019. A comparison of thick-film microscopy, rapid diagnostic test, and polymerase chain reaction for accurate diagnosis of *Plasmodium falciparum* malaria. *Malaria Journal,* 18**,** 73-80.

Misni, N., Nor, Z. & Ahmad, R. 2017. Repellent effect of microencapsulated essential oil in lotion formulation against mosquito bites. *Journal Of Vector Borne Diseases,* 54**,** 44-53.

Mitra, S., Rodriguez, S. D., Vulcan, J., Cordova, J., Chung, H.-N., Moore, E., et al. 2019. Efficacy of Active Ingredients From the EPA 25(B) List in Reducing Attraction of *Aedes aegypti* (Diptera: Culicidae) to Humans. *Journal Of Medical Entomology,* 57**,** 477-484.

Mmbando, A. S., Batista, E. P., Kilalangongono, M., Finda, M. F., Mwanga, E. P., Kaindoa, E. W., et al. 2019. Evaluation of a push–pull system consisting of transfluthrin-treated eave ribbons and odour-baited traps for control of indoor-and outdoor-biting malaria vectors. *Malaria Journal,* 18**,** 87-200.

ModernDayProductLLC. 2020. *Mosquito guard repellent stickers/patches for kids (60 pack) made with natural plant based ingredients - citronella, lemongrass, geraniol - deet free* [Online]. Available: https://www.ubuy.za.com/search/index/view/product/B07RKYTT1G/s/mosquito-guard-repellent-stickers-patches-for-kids-60-pack-made-with-natural-plant-based-ingredients-citronella-lemongrass-geraniol-deet-free/store/store/kk/dp?ref_p=dp-rp [Accessed 26/04/ 2020].

Mokuolu, O. A., Ntadom, G. N., Ajumobi, O. O., Alero, R. A., Wammanda, R. D., Adedoyin, O. T., et al. 2016. Status of the use and compliance with malaria rapid diagnostic tests in formal private health facilities in Nigeria. *Malaria Journal,* 15**,** 4-14.

Moore, B. R., Benjamin, J. M., Tobe, R., Ome-Kaius, M., Yadi, G., Kasian, B., et al. 2019. A randomized open-label evaluation of the antimalarial prophylactic efficacy of azithromycin-piperaquine versus sulfadoxine-pyrimethamine in pregnant Papua

New Guinean women. *Antimicrobial Agents And Chemotherapy,* 63**,** e00302-e00312.

Moonasar, D., Davies, C., Balawanth, R., Misiani, E., Shandukani, M., Raman, J., et al. 2021. Progress, challenges and priorities for malaria elimination in South Africa. *TRANSACTIONS OF THE ROYAL SOCIETY OF SOUTH AFRICA,* 76**,** 105-116.

Moore, S. J., Lenglet, A. & Hill, N. 2002. Field evaluation of three plant-based insect repellents against malaria vectors in Vaca Diez Province, the Bolivian Amazon. *Journal Of The American Mosquito Control Association,* 18**,** 107-110.

Moyeh, M. N., Ali, I. M., Njimoh, D., #Xe9, L., Nji, A. M., et al. 2019. Comparison of the accuracy of four malaria diagnostic methods in a high transmission setting in Coastal Cameroon. *Journal Of Parasitology Research,* 2019**,** 1-9..

Mukherjee, G. & Ghosh, S. 2020. Use of cow dung as mosquito repellant. *International Research Journal Of Pharmacy And Medical Science,* 3**,** 61-62.

Mulla, M. S., Thavara, U., Tawatsin, A., Kong-Ngamsuk, W. & Chompoosri, J. 2001. Mosquito burden and impact on the poor: Measures and costs for personal protection in some communities in Thailand. *Journal Of The American Mosquito Control Association,* 17**,** 153-159.

Munhenga, G., Oliver, S. V., Lobb, L. N., Mazarire, T. T., Sekgele, W., Mashatola, T., et al. 2022. Malaria risk and receptivity: Continuing development of insecticide resistance in the major malaria vector Anopheles arabiensis in northern KwaZulu-Natal, South Africa. *SOUTH AFRICAN JOURNAL OF SCIENCE,* 118**,** 1-7.

Munzhedzi, M., Rogawski Mcquade, E. T., Guler, J. L., Shifflett, P. E., Krivacsy, S., Dillingham, R., et al. 2021. Community knowledge, attitudes and practices towards malaria in Ha-Lambani, Limpopo Province, South Africa: a cross-sectional household survey. *Malaria Journal,* 20**,** 188-193.

Murphy'sNaturalsInc. 2020. *Murphy's naturals mosquito repellent incense sticks | deet free with plant based ingredients | 2.5 hour protection | 8 sticks per carton* [Online]. Available: https://www.ubuy.za.com/search/index/view/product/B0754LHVZR/s/murphy-s-naturals-mosquito-repellent-incense-sticks-deet-free-with-plant-based-ingredients-2-5-hour-protection-8-sticks-per-carton/store/store/kk/dp?ref_p=dp-rp [Accessed 26/04/ 2020].

Murray, C. K., Gasser, R. A., Magill, A. J. & Miller, R. S. 2008. Update on rapid diagnostic testing for malaria. *Clinical Microbiology Reviews,* 21**,** 97-110.

Mwesigwa, J., Slater, H., Bradley, J., Saidy, B., Ceesay, F., Whittaker, C., et al. 2019. Field performance of the malaria highly sensitive rapid diagnostic test in a setting of varying malaria transmission. *Malaria Journal,* 18**,** 288-291.

Nattee, C., Khamsemanan, N., Lawtrakul, L., Toochinda, P. & Hannongbua, S. 2017. A novel prediction approach for antimalarial activities of Trimethoprim, Pyrimethamine, and Cycloguanil analogues using extremely randomized trees. *Journal Of Molecular Graphics And Modelling,* 71**,** 13-27.

Naucke, T., Kröpke, R., Benner, G., Schulz, J., Wittern, K., Rose, A., et al. 2007. Field evaluation of the efficacy of proprietary repellent formulations with IR3535® and Picaridin against *Aedes aegypti. Parasitology Research,* 101**,** 169-177.

Navaratnam, V., Mahsufi Mansor, S., Sit, N.-W., Grace, J., Li, Q. & Olliaro, P. 2000. Pharmacokinetics of Artemisinin-Type Compounds. *Clinical Pharmacokinetics,* 39**,** 255-270.

Newchic. 2019. *Ultrasonic mosquito repellent electronic insect repeller home intelligent electronic fly repeller* [Online]. Available: https://za.newchic.com/minleaf-pests-control-and-killer-4919/p-1519267.html?gmcCountry=ZA&currency=ZAR&createTmp=1&ID=516220&utm_source=googleshopping&utm_medium=shopping&utm_campaign=pla-ssc-gjz-za3-all-15-nca&utm_content=warren&gclid=CjwKCAiAuqHwBRAQEiwAD-zr3WD1w4qakfmF-YEkluGQ4OZ4O7H5comakMMBdyyNJOaDn1BdE0rF9BoCP6oQAvD_BwE [Accessed 29/12/ 2019].

Newchic. 2020. *100 pcs riddex plant seeds mosquito repelling grass mozzie buster sweetgrass. Garden & home bonsai* [Online]. Available: https://za.newchic.com/egrow-grasses-8677/p-1266812.html?gmcCountry=ZA&currency=ZAR&createTmp=1&utm_source=googleshopping&utm_medium=shopping&utm_campaign=pla-ssc-gjz-za3-all-15-nca&utm_content=warren&gclid=Cj0KCQjw9tbzBRDVARIsAMBplx8NBA14OL7LCT8hUBadIw8RK3RGT_34Ww-ZK3IaznEkwYbH-xOC9NsaArNXEALw_wcB [Accessed 21/03/ 2020].

Ngasala, B., Mutemi, D. D. & Mwaiswelo, R. O. 2019. Diagnostic performance of malaria rapid diagnostic test and microscopy compared with pcr for detection of *Plasmodium falciparum* infections among primary schoolchildren in kibiti district, eastern Tanzania: An area with moderate malaria transmission. *The American Journal Of Tropical Medicine And Hygiene,* 101**,** 809-811.

Nguyen, Q.-B. D., Vu, M.-A. N. & Hebert, A. A. 2018. Insect repellents: An updated review for the clinician. *Journal of the American Academy of Dermatology. doi: https://doi.org/10.1016/ j.jaad.2018.10.053.***,** 1-19.

Njau, J., Silal, S. P., Kollipara, A., Fox, K., Balawanth, R., Yuen, A., et al. 2021. Investment case for malaria elimination in South Africa : a financing model for resource mobilization to accelerate regional malaria elimination. *Malaria Journal,* 20**,** 344-359.

Njumkeng, C., Apinjoh, T. O., Anchang-Kimbi, J. K., Amin, E. T., Tanue, E. A., Njua-Yafi, C., et al. 2019. Coverage and usage of insecticide treated nets (ITNs) within households : associated factors and effect on the prevalance of malaria parasitemia in the Mount Cameroon area. *BMC Public Health,* 19**,** 1216-1226.

Nkegbe, P. K., Kuunibe, N. & Sekyi, S. 2017. Poverty and malaria morbidity in the Jirapa District of Ghana: A count regression approach. *Cogent Economics & Finance,* 5**,** 1293472-1293484.

Noedl, H., Se, Y., Schaecher, K., Smith, B. L., Socheat, D. & Fukuda, M. M. 2008. Evidence of artemisinin-resistant malaria in Western Cambodia. *New England Journal Of Medicine,* 359**,** 2619-2620.

Norris, E. J. & Coats, J. R. 2017. Current and future repellent technologies: The potential of spatial repellents and their place in mosquito-borne disease control. *International Journal Of Environmental Research And Public Health,* 14**,** 124-138.

Nwaneri, D. & Sadoh, A. 2020. Effect of health seeking behaviour of caregivers on severe malaria outcome in under-fives seen in a tertiary health institution in nigeria. *Ghana Medical Journal,* 54**,** 156-163.

O'Neill, P. M., Barton, V. E. & 2, S. A. W. 2010. The molecular mechanism of action of artemisinin—the debate continues. *Molecules,* 15**,** 1705-1721.

Oboh, M. A., Badiane, A. S., Ntadom, G., Ndiaye, Y. D., Diongue, K., Diallo, M. A., et al. 2018. Molecular identification of *Plasmodium* species responsible for malaria

reveals *Plasmodium* vivax isolates in duffy negative individuals from Southwestern Nigeria. *Malaria Journal,* 17**,** 439-450.

Ogillo, K. I., Lyaruu, L., Lyatuu, E., Mahande, A. & Kweka, E. J. 2016. Comparative Efficiency of Four Repellents against A*nopheles gambiae* ss. *Journal Of Mosquito Research,* 6-12.

Ogoma, S. B., Moore, S. J. & Maia, M. F. 2012. A systematic review of mosquito coils and passive emanators: Defining recommendations for spatial repellency testing methodologies. *Parasites & Vectors,* 5**,** 287-296.

Oguntade, E. S., Shohaimi, S., Nallapan, M. & Lamidi-Sarumoh, A. A. 2018. Factors influencing malaria knowledge, attitude and practice in Gwagwalada. *INTERNATIONAL Journal Of Science & Healthcare Research,* 3**,** 168-178.

Okafor, I. P., Ezekude, C., Oluwole, E. O. & Onigbogi, O. O. 2019. Malaria in pregnancy: A community-based study on the knowledge, perception, and prevention among Nigerian women. *J FAMILY MED PRIM CARE,* 8**,** 1359-1364.

Okwa, O. O. 2019. *Nipping the malaria vectors in the bud: Focus on nigeria* [Online]. IntechOpen. Available: https://books.google.com.ng/books?hl=en&lr=&id=qmX8DwAAQBAJ&oi=fnd&pg=PA91&dq=Okwa,+O.+O.+2019.+Nipping+the+malaria+vectors+in+the+bud:+Focus+on+nigeria.+Malaria.+IntechOpen.&ots=NJu7efBM52&sig=ltlWaLh74IT3SAKeza47FWQ8jaU&redir_esc=y#v=onepage&q=Okwa%2C%20O.%20O.%202019.%20Nipping%20the%20malaria%20vectors%20in%20the%20bud%3A%20Focus%20on%20nigeria.%20Malaria.%20IntechOpen.&f=false [Accessed 04/05/ 2020].

Okwa, O., Bello, B. & Olundegun, S. 2011. Social aspects of malaria among students in two tertiary institutions in Lagos, Nigeria. *Sierra Leone Journal Of Biomedical Research,* 3**,** 97-103.

Okwa, O., Soremekun, B., Adeseko, O. & Raheem, A. 2012. Artisans and traders' knowledge, attitude and practices of malaria in selected areas of Lagos, Nigeria. *Mechanics,* 14**,** 16-22.

Oladimeji, K. E., Tsoka-Gwegweni, J. M., Ojewole, E. & Yunga, S. T. 2019. Knowledge of malaria prevention among pregnant women and non-pregnant mothers of children aged under 5 years in Ibadan, South West Nigeria. *Malaria Journal,* 18**,** 92-104.

Olanrewaju, W. & Johnson, A.-W. 2001. Malaria in children in Ilorin, Nigeria. *East African Medical Journal,* 78**,** 131-134.

Olaosebikan, V. O., Alabi, O., Hussaini, K. & Ojo, A. A. 2020. In the absence of effective malaria parasite sentinel system: A cross-sectional study to assess prevalence of *Plasmodium s*pp infection and malaria among patients at Federal Medical Centre Birnin-Kebbi, Kebbi State, Nigeria. *Reseaech Square,* 1**,** 1-10.

Olayemi, I. K., Omalu, I. C., Abolarinwa, S. O., Mustapha, A. V., Ayanwale, V. A., Mohammed, A. Z., et al. 2012. Knowledge of malaria and implications for control in an endemic urban area of north central Nigeria. *Asian Journal Of Epidemiology,* 5**,** 42-49.

Omarland, L. & Vythilingam, L. O. I. Laboratory evaluation of three herbal repellents against mosquitoes of public health importance in Malaysia. *Tropical Biomedicine*, 9, 61-65.

O'Neal, S. T., Johnson, E. J., Rault, L. C. & Anderson, T. D. 2019. Vapor delivery of plant essential oils alters pyrethroid efficacy and detoxification enzyme activity in mosquitoes. *Pesticide Biochemistry And Physiology,* 157**,** 88-98.

Onile-ere, O., Openibo, J. & Olasehinde, G. Malaria diagnosis: Current approaches and future prospects. International Conference On African Development Issues (CU-ICADI), 2016 Covenant University, Ota, Nigeria. . 314-319.

Onwujekwe, O., Uzochukwu, B., Dike, N., Uguru, N., Nwobi, E. & Shu, E. 2009. Malaria treatment perceptions, practices and influences on provider behaviour: Comparing hospitals and non-hospitals in South-East Nigeria. *Malaria Journal,* 8**,** 246-253.

Ouologuem, D. T., Kone, C. O., Fofana, B., Sidibe, B., Togo, A. H., Dembele, D., et al. 2018. Differential infectivity of gametocytes after artemisinin-based combination therapy of uncomplicated falciparum malaria. *African Journal Of Laboratory Medicine,* 7**,** 1-6.

OutDoorWarehousforeveryadventure. 2020a. *Coghlan's citronella candle* [Online]. Available: https://www.outdoorwarehouse.co.za/product/coghlans-citronella-candle/6431 [Accessed 25/04/ 2020].

OutDoorWarehousforeveryadventure. 2020b. *Fever tree fly and mosquito repellent 250g* [Online]. Available: https://www.outdoorwarehouse.co.za/product/fever-tree-fly-and-mosquito-repellent-250g/6431 [Accessed 24/04/ 2020].

OutDoorWarehousforeveryadventure. 2020c. *Fever tree non-toxic liquid plug-in combo pack* [Online]. Available: https://www.outdoorwarehouse.co.za/product/fever-tree-non-toxic-liquid-plug-in-combo-pack/6431 [Accessed 24/04/ 2020].

OutDoorWarehousforeveryadventure. 2020d. *Lifetrek mosquito band kids 2 pk* [Online]. Available: https://www.outdoorwarehouse.co.za/product/lifetrek-mosquito-band-kids-2-pk-1/6431 [Accessed 24/04/ 2020].

OutDoorWarehousforeveryadventure. 2020e. *Republic umbrella citronella mosquito repellant candle (300g)* [Online]. Available: https://www.outdoorwarehouse.co.za/product/republic-umbrella-citronella-mosquito-repellant-candle-300g/6431 [Accessed 25/04/ 2020].

OutDoorWarehousforeveryadventure. 2020f. *Republic umbrella citronella table lamp* [Online]. Available: https://www.outdoorwarehouse.co.za/product/republic-umbrella-citronella-table-lamp/6431 [Accessed 25/04/ 2020].

OutDoorWarehousforeveryadventure. 2020g. *Tabard candle medium 240g* [Online]. Available: https://www.outdoorwarehouse.co.za/product/tabard-medium-candle/6431 [Accessed 25/04/ 2020].

OutDoorWarehousforeveryadventure. 2020h. *Tabard candle small 120g* [Online]. Available: https://www.outdoorwarehouse.co.za/product/tabard-small-candle/6431 [Accessed 25/04/ 2020].

OutDoorWarehousforeveryadventure. 2020i. *Tabard stick 30ml* [Online]. Available: https://www.outdoorwarehouse.co.za/product/tabard-stick/6431 [Accessed 25/04/ 2020].

Oyibo WA, Ezeigwe N, Ntadom G, Oladosu OO, Rainwater-Loveth K, O'Meara W, Okpokoro E, Brieger W. 2016. Multicenter Pivotal Clinical Trial of Urine Malaria Test for Rapid Diagnosis of *Plasmodium falciparum* Malaria. *Journal Of Clinical Microbiology*. 55(1):253-263.

Padonou, G. G., Gbenoudon, J. G., Osse, R., Salako, A., Kpanou, C., Sagbohan, H., et al. 2018. Knowledge-Attitudes-Practices about Malaria among Communities in Southern Benin. *International Journal Of Public Health,* 7**,** 186–193.

Pagar, K. R. & Khandbahale, S. V. 2020. Antimalarial drug toxicity: A review. *International Journal Of PharmaO2,* 1**,** 0044-0056.

Patel, R. V., Shaeer, K. M., Patel, P., Garmaza, A., Wiangkham, K., Franks, R. B., et al. 2016. EPA-registered repellents for mosquitoes transmitting emerging viral disease. *Pharmacotherapy: The Journal Of Human Pharmacology And Drug Therapy,* 36**,** 1272-1280.

Pavela, R. & Benelli, G. 2016. Ethnobotanical knowledge on botanical repellents employed in the African region against mosquito vectors – a review. *Experimental Parasitology,* 167**,** 103-108.

Pavela, R., Maggi, F., Giordani, C., Cappellacci, L., Petrelli, R. & Canale, A. 2020. Insecticidal activity of two essential oils used in perfumery (ylang ylang and frankincense). *Natural Product Research***,** 1-7.

Pawar, S., Gujar, M., Yadav, P., Supugade, V. & Patil, R. 2019. Use of various plant extracts as herbal mosquito repellent spray. *Global Journal For Research Analysis (Gjra),* 8**,** 33-34.

PCLinksComputers. 2020. *Bundle of 2 sallyeander products - no-bite-me soap and creme - deet-free - all natural, kid safe* [Online]. Available: https://pclinkshop.com/products/bundle-of-2-sallyeander-products-no-bite-me-soap-and-creme-deet-free-all-natural-kid-safe?utm_source=Click&utm_medium=Channel&utm_campaign=PriceCheck_ZA&ref=SFDR_690780091&variant=29083840675884&ptcid=19517_1_503758502 [Accessed 24/04/ 2020].

Pell, C. L., Adhikari, B., Myo Thwin, M., Kajeechiwa, L., Nosten, S., Nosten, F. H., et al. 2019. Community engagement, social context and coverage of mass anti-malarial administration: Comparative findings from multi-site research in the Greater Mekong sub-Region. *Public Library Of Science One,* 14**,** E0214280-e0214413.

Petchimuthu, R., Clayton Fernando, R., Anand, G., Gowtham, P., Dhivagar, K. & Vanavil, B. 2019. Assessment of efficiency of eco-friendly organic mosquito repellent developed using Elephant dung. *International Journal Of Recent Technology And Engineering (Ijrte)* 8**,** 459-462.

Pett, H., Gonçalves, B. P., Dicko, A., Nébié, I., Tiono, A. B., Lanke, K., et al. 2016. Comparison of molecular quantification of *Plasmodium falciparum* gametocytes by Pfs25 qRT-PCR and QT-NASBA in relation to mosquito infectivity. *Malaria Journal,* 15**,** 539-549.

Pikitup. 2018. *Some see waste* [Online]. Available: https://www.joburg.org.za/departments_/Pages/MOEs/Pikitup.aspx [Accessed 15/04/ 2022].

PlatTechnologies. 2020. *Nigeria directory - Sir Yahaya Memorial Hospital, Kebbi* [Online]. Available: https://www.directory.org.ng/directory_sir_yahaya_memorial_hospital_kebbi [Accessed 05/02/ 2022].

Plewes, K., Leopold, S. J., Kingston, H. W. F. & Dondorp, A. M. 2019. Malaria: What's New in the Management of Malaria? *Infectious Disease Clinics Of North America,* 33**,** 39-60.

Plucinski, M. M., Candrinho, B., Dimene, M., Colborn, J., Lu, A., Nace, D., et al. 2019. Assessing Performance of HRP2 Antigen Detection for Malaria Diagnosis in Mozambique. *Journal Of Clinical Microbiology,* 57**,** E00875-e00894.

Prah, J. K., Yeboah-Sarpong, A., Pinkrah, R. & Ewudzi-Acquah, E. 2019. Assessment of the knowledge, attitude and practices of prescribers regarding malaria diagnosis: A cross sectional study among Ghanaian prescribers. *The Pan African Medical Journal,* 34**,** 1-10.

PROGUARDNATURA. 2020. *Mosquito repellent spray and cream* [Online]. Available: http://www.proguardnatura.co.za/products_mosquito_repellents.php [Accessed 26/04/ 2020].

Raja, T. N., Hu, T. H., Kadir, K. A., Mohamad, D. S. A., Rosli, N., Wong, L. L., et al. 2020. Naturally Acquired Human *Plasmodium cynomolgi* and *P. knowlesi* Infections, Malaysian Borneo. *Emerging Infectious Diseases,* 26**,** 1801-1809.

Raman, J., Gast, L., Balawanth, R., Tessema, S., Brooke, B., Maharaj, R., et al. 2020. High levels of imported asymptomatic malaria but limited local transmission in KwaZulu-Natal, a South African malaria-endemic province nearing malaria elimination. *Malaria Journal,* 19**,** 1–13.

Ramharter, M., Schwab, M., Mombo-Ngoma, G., Manego, R. Z., Akerey-Diop, D., Basra, A., et al. 2019. Population pharmacokinetics of mefloquine intermittent preventive treatment for malaria in pregnancy in Gabon. *Antimicrobial Agents And Chemotherapy,* 63**,** e01113-e01131.

Ray, A. 2015. Reception of odors and repellents in mosquitoes. *Current Opinion In Neurobiology,* 34**,** 158-164.

Ray, S. & Nair, S. 2011. Do health care providers adhere to the revised malaria control guidelines? *International Journal Of Collaborative Research On Internal Medicine & Public Health,* 3**,** 752-779.

RBM. 2019. *Key facts about malaria* [Online]. Available: https://endmalaria.org/about-malaria/key-facts [Accessed 19/04/ 2020].

Rehman, J. U., Ali, A. & Khan, I. A. 2014. Plant based products: Use and development as repellents against mosquitoes: A Review. *Fitoterapia,* 95**,** 65–74.

Reichert, W., Ejercito, J., Guda, T., Dong, X., Wu, Q., Ray, A., et al. 2019. Repellency Assessment of *Nepeta cataria* Essential Oils and Isolated Nepetalactones on *Aedes aegypti. Scientific Reports,* 9**,** 1524-1533.

REPEL. 2020a. *Repel lemon aerosol eucalyptus insect repellent, 4 oz + 2 bonus wipes* [Online]. Available: https://www.ubuy.za.com/search/index/view/product/B07P5PGHN8/s/repel-lemon-aerosol-eucalyptus-insect-repellent-4-oz-2-bonus-wipes/store/store/kk/dp?ref_p=dp-rp [Accessed 26/04/ 2020].

REPEL. 2020b. *Repel permethrin clothing & gear insect repellent, aerosol, 6.5-ounce* [Online]. Available: https://www.ubuy.za.com/search/index/view/product/B00AA8WX52/s/repel-permethrin-clothing-gear-insect-repellent-aerosol-6-5-ounce/store/store/kk/dp?ref_p=dp-rp [Accessed 26/04/ 2020].

REPEL. 2020c. *Repel sportsmen max aerosol insect repellent bonus, 40% deet, 8.125 oz - 2 count - with bonus healthandoutdoors moist towelettes* [Online]. Available: https://www.ubuy.za.com/search/index/view/product/B07DNKF34T/s/repel-sportsmen-max-aerosol-insect-repellent-bonus-40-deet-8-125-oz-2-count-with-bonus-healthandoutdoors-moist-towelettes/store/store/kk/dp?ref_p=dp-rp [Accessed 26/04/ 2020].

Rodrigues, K. M. d. P., Costa, A. B. F. d. & Santoro-Lopes, G. 2019. Adherence to malaria prophylaxis among travelers from a middle-income country. *Revista Da Sociedade Brasileira De Medicina Tropical,* 52**,** 1-5.

Rodriguez, S. D., Chung, H.-N., Gonzales, K. K., Vulcan, J., Li, Y., Ahumada, J. A., et al. 2017. Efficacy of some wearable devices compared with spray-on insect repellents for the yellow fever mosquito, *Aedes aegypti* (L.) (Diptera : Culicidae). *Journal Of Insect Science,* 17**,** 1-6.

Rosenthal, P. J. 2017. Antiprotozoal drugs. *In:* Katzung, B. G. (ed.) *Basic and Clinical Pharmacology, 14e.* New York, NY: McGraw-Hill Education.

Rosenthal, P. J. 2018. Artemisinin resistance outside of Southeast Asia. *The American Journal Of Tropical Medicine And Hygiene,* 99**,** 1357-1359.

Rowe, A. K., de Savigny, D., Lanata, C. F. & Victora, C. G. 2005. How can we achieve and maintain high-quality performance of health workers in low-resource settings? *The Lancet, 366, 1026-1035.*

Rupérez, M., González, R., Mombo-Ngoma, G., Kabanywanyi, A. M., Sevene, E., Ouédraogo, S., et al. 2016. Mortality, morbidity, and developmental outcomes in infants born to women who received either mefloquine or sulfadoxine-pyrimethamine as intermittent preventive treatment of malaria in pregnancy: a cohort study. *Plos Medicine,* 13**,** 1-18.

SADOH. 2018. *South African Department of Health Guidelines For The Treatment Of Malaria In South Africa 2018 update* [Online]. Available: https://wakelet.com/wake/wG9JgiXEMrzjjbGpWK9MZ [Accessed 15/10/ 2019].

SADOH. 2019. *South African Department of Health National Guidelines For The Treatment Of Malaria, South Africa 2019* [Online]. Available: https://wakelet.com/wake/wG9JgiXEMrzjjbGpWK9MZ [Accessed 15/10/ 2019].

SAHPRA. 2022. *SAHPRA registered health products* [Online]. Available: https://registered-health-products.sahpra.org.za [Accessed 15/01/ 2022].

Samuel, M., Qwabe, B., Dlamini, D., Mabaso, N., Manyawo, Z., Zhikali, J., et al. 2018. Malaria vector surveillance report, South Africa, January–December 2018. *Johannesburg: National Institute For Communicable Diseases Bulletin,* 17**,** 47-59.

Sanford, J. L., Shields, V. D. & Dickens, J. C. 2013. Gustatory receptor neuron responds to deet and other insect repellents in the yellow-fever mosquito, *Aedes aegypti. Naturwissenschaften,* 100**,** 269-273.

SDGs. 2017. *Sustainable development goal 3, ensure healthy lives and promote well-being for all at all ages* [Online]. Available: https://sustainabledevelopment.un.org/hlpf/2017 [Accessed 16/10/ 2019].

Setzer, W. N. 2016. Catnip essential oil: There is more to it than making your cat go crazy. *American Journal of Essential Oils and Natural Products,* 4**,** 12-15.

Shisana, O., Labadarios, D., Rehle, T., Simbayi, L., Zuma, K., Dhansay, A., et al. 2014. *The South African National Health and Nutrition Examination Survey, 2012: SANHANES-1: the health and nutritional status of the nation* [Online]. Available: http://repository.hsrc.ac.za/handle/20.500.11910/2864 [Accessed 28/05/ 2020].

Shukla, D., Wijayapala, S. & Vankar, P. S. 2018. Effective mosquito repellent from plant based formulation. *International Journal Of Mosquito Research,* 5**,** 19-24.

Simon, J. E., Reichert, W. & Wu, Q. 2019. *Catnip cultivar 'cr3'* [Online]. Google Patents. Available: https://patents.google.com/patent/US10512231B2/en [Accessed 29/01/ 2020].

Singh, B., Sung, L. K., Matusop, A., Radhakrishnan, A., Shamsul, S. S. G., Cox-Singh, J., et al. 2004. A large focus of naturally acquired *Plasmodium knowlesi* infections in human beings. *The Lancet, 3*63**,** 1017-1024.

Slater, H. C., Griffin, J. T., Ghani, A. C. & Okell, L. C. 2016. Assessing the potential impact of artemisinin and partner drug resistance in Sub-Saharan Africa. *Malaria Journal, 15***,** 10-20.

Songkro, S., Yapong, P., Puechpan, P., Maneenuan, D. & Boonme, P. 2018. Microencapsulation of citronella oil for mosquito repellent: Preparation and evaluation of release characteristics*. Songklanakarin Journal Of* Science *And* Technology*,* 40**,** 767-775.

Sparks, J. T. & Dickens, J. C. 2016. Electrophysiological responses of gustatory receptor neurons on the labella of the common malaria mosquito, *Anopheles quadrimaculatus* (diptera: Culicidae)*. Journal Of Medical Entomology,* 53**,** 1148-1155.

Stringer, T., Wiesner, L. & Smith, G. S. 2019. Ferroquine-derived polyamines that target resistant *Plasmodium falciparum*. *European Journal Of Medicinal Chemistry,* 179**,** 78-83.

Sukumaran, D. 2016. A review on use of attractants and traps for host seeking *Aedes aegypti* mosquitoes. *Indian Journal Of Natural Products And Resources (Ijnpr)[Formerly Natural Product Radiance (Npr)], 7, 207-214.*

Sumari, D., Dillip, A., Ndume, V., Mugasa, J. P. & Gwakisa, P. S. 2016. Knowledge, attitudes and practices on malaria in relation to its transmission among primary school children in Bagamoyo District, Tanzania*. Malaria World Journal,* 7**,** 1-8.

Sureshkumar, B., Mary, Y. S., Panicker, C. Y., Suma, S., Armaković, S., Armaković, S. J., et al. 2020. Quinoline derivatives as possible lead compounds for anti-malarial drugs: Spectroscopic, DFT and MD study. *Arabian Journal Of Chemistry,* 13**,** 632-648.

Swale, D. R. & Bloomquist, J. R. 2019. Is DEET a dangerous neurotoxicant? *Pest Management Science,* 75**,** 2068-2070.

Swale, D. R., Sun, B., Tong, F. & Bloomquist, J. R. 2014. Neurotoxicity and mode of action of N, N-diethyl-meta-toluamide (DEET). *Plos One,* 9**,** e103713-e103723.

Szumilas, M. 2010. Explaining odds ratios. *Journal of the Canadian Academy of Child and Adolescent Psychiatry. Journal de l'Académie Canadienne de Psychiatrie de L'enfant et de l'Adolescent,* 19**,** 227-9.

Ta, T. H., Hisam, S., Lanza, M., Jiram, A. I., Ismail, N. & Rubio, J. M. 2014. First case of a naturally acquired human infection with *Plasmodium cynomolgi*. *Malaria Journal,* 13**,** 68-73.

TABARD. 2020. *Tabard fabric guard insect repellent* [Online]. Available: http://tabard.co.za/#iLightbox[gallery_image_1]/1 [Accessed 26/04/ 2020].

TAKEALOT. 2020a. *Reitzer camp/outdoor soap glyc.2pk* [Online]. Available: https://www.takealot.com/reitzer-camp-outdoor-soap-glyc-2pk/PLID27832889?gclid=CjwKCAjwv4_1BRAhEiwAtMDLsu7cC-ygDYPdsay-NeJgwsLZDl3fHqaGmFLcYCT4IIVoyr1fX9YKKhoCXSoQAvD_BwE&gclsrc=aw.ds [Accessed 25/04/ 2020].

TAKEALOT. 2020b. *Robosol auto insect control for flies & mosquitoes* [Online]. Available: https://www.takealot.com/robosol-auto-insect-control-for-flies-mosquitoes/PLID46868218?gclid=CjwKCAjw4pT1BRBUEiwAm5QuR-TtDcwyaWpsSs1xOqlo_b2iUrJWSyuPoOBh8XxQXVU30ju9Xp2zuhoCxvEQAvD_BwE&gclsrc=aw.ds [Accessed 26/04/ 2020].

Talman, A. M., Clain, J., Duval, R., Ménard, R. & Ariey, F. 2019. Artemisinin bioactivity and resistance in malaria parasites. *Trends In Parasitology***,** 1-11.

Tambo, M., Mwinga, M. & Mumbengegwi, D. R. 2018. Loop-mediated isothermal amplification (LAMP) and Polymerase Chain Reaction (PCR) as quality assurance tools for Rapid Diagnostic Test (RDT) malaria diagnosis in Northern Namibia. *Public Library Of Science One,* 13**,** E0206848-E0206856.

Tangpukdee, N., Duangdee, C., Wilairatana, P. & Krudsood, S. 2009. Malaria diagnosis: A brief review. *The Korean Journal Of Parasitology,* 47**,** 93-102.

Tangpukdee, N., Krudsood, S., Srivilairit, S., Phophak, N., Chonsawat, P., Yanpanich, W., et al. 2008. Gametocyte clearance in uncomplicated and severe *Plasmodium falciparum* malaria after artesunate-mefloquine treatment in Thailand. *The Korean Journal Of Parasitology,* 46**,** 65-70.

Tao, D., Mcgill, B., Hamerly, T., Kobayashi, T., Khare, P., Dziedzic, A., et al. 2019. A saliva-based rapid test to quantify the infectious subclinical malaria parasite reservoir. *Science Translational Medicine,* 11**,** eaan4479-eaan4492.

Tavares, E. M., Judge, B. S. & Jones, J. S. 2019. Bug off! Severe toxicity following inhalational exposure to N, N-Diethyl-meta-toluamide (DEET). *The American Journal Of Emergency Medicine,* 37**,** 1395.e3-1395.e4.

Tavares, M., Da Silva, M. R. M., De Oliveira De Siqueiros, L. B., Rodrigues, R. a. S., Bodjolle-D'almeida, L., Dos Santos, E. P., et al. 2018. Trends in insect repellent formulations : A review. *International Journal Of Pharmaceutics,* 539**,** 190-209.

Teklemariam, A. 2018. Community's knowledge, attitude and practices toward malaria And Mosquito Behavior In Abeshige Woreda, Gurage Zone, Southern Ethiopia. *The Journal Of Parasitology And Vector Biology,* 10**,** 145-155.

Teo, A., Randall, L. M., Madanitsa, M., Mwapasa, V., Phiri, L. K., Khairallah, C., et al. 2019. Intermittent screening and treatment with dihydroartemisinin-piperaquine and intermittent preventive therapy with sulfadoxine-pyrimethamine have similar effects on malaria antibody in pregnant Malawian women. *Scientific Reports,* 9**,** 7878-7888.

Thireou, T., Kythreoti, G., Tsitsanou, K. E., Koussis, K., Drakou, C. E., Kinnersley, J., et al. 2018. Identification of novel bioinspired synthetic mosquito repellents by combined ligand-based screening and OBP-structure-based molecular docking. *Insect Biochemistry And Molecular Biology,* 98**,** 48-61.

Thorsell, W., Mikiver, A., Malander, I. & Tunon, H. 1998. Efficacy of plant extracts and oils as mosquito repellents. *Phytomedicine,* 5**,** 311-323.

Tian, Y., Dong, F., Zhou, X. & Yang, X. 2020. Repellent, insecticidal and antimicrobial activities of leaf essential oils from three *Eucalyptus* species. *Chemistry & Biodiversity. Doi:10.1002/Cbdv.201900580***,** 1-16.

TIPS, S. A. D. A. Y. F. 2002a. *Charlotte Maxeke Johannesburg Academic Hospital - Parktown, Gauteng, South Africa* [Online]. Available: http://doctors-hospitals-medical-cape-town-south-africa.blaauwberg.net/hospitals_clinics_state_hospitals/state_public_hospitals_clinics_gauteng_south_africa/charlotte_maxeke_johannesburg_academic_hospital_parktown_gauteng_south_africa [Accessed 3/04 2019].

TIPS, S. A. D. A. Y. F. 2002b. *Helen Joseph Hospital - Auckland Park, Johannesburg, Gauteng, South Africa* [Online]. Available: http://doctors-hospitals-medical-cape-town-south-africa.blaauwberg.net/hospitals_clinics_state_hospitals/state_public_hospitals_clinics_gauteng_south_africa/helen_joseph_hospital_auckland_park_johannesburg_gauteng_south_africa [Accessed 03/04/ 2019].

Tisgratog, R., Sanguanpong, U., Grieco, J. P., Ngoen-Kluan, R. & Chareonviriyaphap, T. 2016. Plants traditionally used as mosquito repellents and the implication for their use in vector control. *Acta Tropica,* 157**,** 136-144.

Torres, K., Bachman, C. M., Delahunt, C. B., Alarcon Baldeon, J., Alava, F., Gamboa Vilela, D., et al. 2018. Automated microscopy for routine malaria diagnosis: a field comparison on Giemsa-stained blood films in Peru. *Malaria Journal,* 17**,** 339-346.

Trongtokit, Y., Curtis, C. F. & Rongsriyam, Y. 2005a. Efficacy of repellent products against caged and free flying *Anopheles stephensi* mosquitoes. *Southeast Asian Journal Of Tropical Medicine And Public Health,* 36**,** 1423-1431.

Trongtokit, Y., Rongsriyam, Y., Komalamisra, N. & Apiwathnasorn, C. 2005b. Comparative repellency of 38 essential oils against mosquito bites. *Phytotherapy Research,* 19**,** 303-309.

Tseng, C.-H., Tung, C.-W., Peng, S.-I., Chen, Y.-L., Tzeng, C.-C. & Cheng, C.-M. 2018. Discovery of pyrazolo [4, 3-c] quinolines derivatives as potential anti-inflammatory agents through inhibiting of no production. *Molecules,* 23**,** 1036-1048.

UBUY. 2020a. *Greenerways organic insect repellent, deet-free, premium, usda organic, non-gmo, natural mosquito-repellent, bug repellant, bug spray, clothing safe, kid safe, pet safe, baby safe, pest control, 16oz* [Online]. Available: https://www.ubuy.za.com/search/index/view/product/B00E3BXVYE/s/greenerways-organic-insect-repellent-deet-free-premium-usda-organic-non-gmo-natural-

mosquito-repellent-bug-repellant-bug-spray-clothing-safe-kid-safe-pet-safe-baby-safe-pest-control-16oz/store/store/kk/dp?ref_p=dp-rp [Accessed 26/04/ 2020].

UBUY. 2020b. *Sawyer products premium insect repellent with 20% picaridin* [Online]. Available: https://www.ubuy.za.com/search/index/view/product/b01g9g9kek/s/sawyer-products-sp576-premium-insect-repellent-with-20-picaridin,-spray,-6-ounce/store/store [Accessed 26/04/ 2020].

UBUY. 2020c. *W4w mosquito repellent coils - outdoor use reaches up to 10 feet - each coil burns for 5-7 hours (three pack contains 12 coils & 6 coil stands)* [Online]. Available: https://www.ubuy.za.com/search/index/view/product/B07C7ZSC8G/s/w4w-mosquito-repellent-coils-outdoor-use-reaches-up-to-10-feet-each-coil-burns-for-5-7-hours-three-pack-contains-12-coils-6-coil-stands/store/store/kk/dp?ref_p=dp-rp [Accessed 26/04 2020].

Udonwa, N. E., Gyuse, A. N. & Etokidem, A. J. 2010. Malaria: Knowledge and prevention practices among school adolescents in a coastal community in Calabar, Nigeria. *African Journal Of Primary Health Care And Family Medicine,* 2**,** 1-4.

Uma, S., Manohar, M., Muthukrishnan, G., Jebamony, K. & Radhakrishnan, S. 2016. Awareness and treatment seeking behaviour of malaria in selected endemic and non-endemic rural areas of Kanyakumari district, Tamilnadu, India. International *Journal Of Community Medicine And Public Health,* 3, 2313-2318.

Umar, M. T., Chika, A. & Jimoh, A. O. 2011. Compliance of primary health care providers to recommendation of artemesinin-based combination therapy in the treatment of uncomplicated malaria in selected primary health care centres in Sokoto, North Western Nigeria. *International Journal of Tropical Medicine,* 6**,** 70-72.

UpToDate. 2019. *Antimalarial drugs: An overview* [Online]. Available: https://www.uptodate.com/contents/antimalarial-drugs-an-overview [Accessed 2/11/ 2019].

Urama, C. E., Manasseh, C. O., Ukwueze, E. R. & Ogbuabor, J. E. 2021. Choices and determinants of malaria treatment seeking behaviour by rural households in Enugu State, South-East Nigeria. *International Journal Of Health Promotion And Education,* 59**,** 156-173.

Usman, R., Umar, A. A., Gidado, S., Gobir, A. A., Obi, I. F., Ajayi, I., et al. 2018. Predictors of malaria Rapid Diagnostic Tests' utilisation among healthcare workers in Zamfara State. *Public Library Of Science One,* 13**,** e0200856-e0200869.https://doi.org/10.1371/journal. pone.0200856.

Vaisakhi, K.S., Kolla, S. & Rao, A. 2017. Comparative study of conventional staining techniques, quantitative buffy coat, immunochromatography methods and molecular methods (gene amplification) for diagnosis of malaria. *INTERNATIONAL Journal Of Current Microbiology And Applied Sciences,* 6**,** 395-409.

Van Benthem, B. H., Khantikul, N., Panart, K., Somboon, P. & Oskam, L. 2006. Knowledge and use of preventive measures against malaria in endemic and non-endemic villages in Northern Thailand. *Southeast Asian Journal Of Tropical Medicine And Public Health,* 37**,** 243-249.

Van Zyl, R. L. 2016. The malaria season is upon us. *South African Family Practice,* 58**,** 68-72.

WantitAll.CO.ZA. 2020. *Radius zone mosquito repellent from Thermacell, Gen 1.0; rechargeable; protects outdoor spaces from insects for up to 6 hours per charge; easy to use, no spray mosquito control, scent-free, deet-free* [Online]. Available: https://www.wantitall.co.za/lawnandgarden/radius-zone-mosquito-repellent-from-thermacell-gen-1-0-rechargeable-protects-outdoor-spaces-from-ins__b075s9stw5?gclid=CjwKCAjw4pT1BRBUEiwAm5QuR3riXcFqel-R79JsDCY1RSs_P216QXgoBbELo4qINp_VZw-r6afozBoCgUAQAvD_BwE [Accessed 26/04/ 2020].

Ward, C., Phillips, A., Oresanya, O., Olisenekwu, G., Arogunade, E., Moukénet, A., et al. 2022. Delivery of seasonal malaria chemoprevention with enhanced infection prevention and control measures during the COVID-19 pandemic in Nigeria, Burkina Faso and Chad: a cross-sectional study. *Malaria Journal,* 21**,** 1-14.

Warsame, M., Hassan, A. M., Hassan, A. H., Jibril, A. M., Khim, N., Arale, A. M., Gomey, A. H., Nur, Z. S., Osman, S. M., Mohamed, M. S., et al. 2019. High therapeutic efficacy of artemether–lumefantrine and dihydroartemisinin–piperaquine for the treatment of uncomplicated falciparum malaria in Somalia. *Malaria Journal,* 18**,** 231-241.

Watentena, A. & Okoye, C. I. 2019. Species specificity of carbon dioxide, 1-octen-3-ol, l-lactic acid and 2-butanone as mosquito chemo-attractants in mosquito surveillance: A review. *International Journal Of Mosquito Research,* 6**,** 138-142.

Webb, C. E. & Hess, I. M. 2016. A review of recommendations on the safe and effective use of topical mosquito repellents. *Public Health Research & Practice,* 26**,** e2651657-e2651661.

White, N. J., van Vugt, M. & Ezzet, F. 1999. Clinical pharmacokinetics and pharmacodynamics and pharmacodynamics of artemether-lumefantrine. *Clinical Pharmacokinetics,* 37**,** 105-25.

WHO. 2009a. *Guidelines for efficacy testing of mosquito repellents for human skin* [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/70072/WHO_HTM_NTD_WHOPES_2009.4_eng.pdf [Accessed 1/4/ 2019].

WHO, 2009b. World Health Organization-Western Pacific Regional Office (WHO-WPRO), USAID | DELIVER PROJECT, Foundation for Innovative New Diagnostics (FIND), Roll Back Malaria Partnership, President's Malaria Initiative (PMI), and UNICEF. July 2009. *Transporting, Storing, and Handling Malaria Rapid Diagnostic Tests at Central and Peripheral Storage Facilities.* Arlington, Va.: USAID | DELIVER PROJECT, Task Order 3; and Manila: WHO-WPRO.

WHO. 2012. *International travel and health - chapter 7* [Online]. Available: https://www.who.int/publications/i/item/9789241580472 [Accessed 14/01/ 2022].

WHO. 2013. *Guidelines for efficacy testing of spartial repellents.* [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/78142/9789241505024_eng.pdf;jsessionid=563BB0BCC6E249377ED46C5E56C33965?sequence=1 [Accessed 14/04/ 2020].

WHO. 2014. *WHO policy brief for the implementation ofintermittent preventive treatment of malaria in pregnancy using sulfadoxine-pyrimethamine (iptp-sp)* [Online]. Available: https://www.who.int/malaria/publications/atoz/iptp-sp-updated-policy-brief-24jan2014.pdf?ua=1 [Accessed 19/02/ 2020].

WHO. 2015a. *Global technical strategy for malaria 2016–2030* [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/176712/9789241564991_eng.pdf;jsessionid=ABEFCC659C58A3782761A77F28479404?sequence=1 [Accessed 15/10/ 2019].

WHO. 2015b. *Guidelines for the treatment of malaria* [Online]. Available: file:///C:/Users/hp/Downloads/guidelines-for-the-treatment-of-malaria-eng.pdf [Accessed 15/10/ 2019].

WHO. 2015c. *Malaria Case Investigators Training* [Online]. Available: https://www.afro.who.int/news/malaria-case-investigators-training [Accessed 24/07/ 2022].

WHO. 2016. *Integrated community case management of malaria* [Online]. Available: https://www.who.int/malaria/areas/community_case_management/overview/en/ [Accessed 17/10/ 2019].

WHO. 2018a. *Artemisinin resistance and artemisinin-based combination therapy efficacy* [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/274362/WHO-CDS-GMP-2018.18-eng.pdf?ua=1 [Accessed 13/11/ 2019].

WHO. 2018b. *Diagnostic testing* [Online]. Available: https://www.who.int/malaria/areas/diagnosis/en/ [Accessed 15/10/ 2019].

WHO. 2018c. *Overview of malaria treatment* [Online]. Available: https://www.who.int/malaria/areas/treatment/overview/en/ [Accessed 15/10/ 2019].

WHO. 2018d. *WHO malaria terminology* [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/208815/WHO_HTM_GMP_2016.6_eng.pdf?sequence=1 [Accessed 25/11/ 2019].

WHO. 2018e. *World malaria report.* [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/275867/9789241565653-eng.pdf?ua=1 [Accessed 3/11/ 2019].

WHO. 2019a. *The e-2020 initiative of 21 malaria-eliminating countries* [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/325304/WHO-CDS-GMP-2019.07-eng.pdf?ua=1 [Accessed 15/11/ 2019].

WHO. 2019b. *Guidelines for malaria vector control* [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/310862/9789241550499-eng.pdf?ua=1 [Accessed 25/11/ 2019].

WHO. 2019c. *Q&A on artemisinin resistance* [Online]. Available: https://www.who.int/malaria/media/artemisinin_resistance_qa/en/ [Accessed 19/11/ 2019].

Who. 2019d. *Travel medicine (6) Bite avoidance* [Online]. Available: https://www.who.int/ith/CHAPTER_6_For_Publication.pdf [Accessed 15/05 2020].

WHO. 2019e. *WHO-CDs-compendium on malaria management.* [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/312082/WHO-CDS-GMP-2019.03-eng.pdf?sequence=1&isAllowed=y [Accessed 29/10/ 2019].

WHO. 2020. *World Malaria Report 2020: 20 years of global progress and challenges* [Online]. Available: https://scholar.google.com/scholar?q=WHO+2020.+World+malaria+report+2020:+20+years+of+global+progress+and+challenges.&hl=en&as_sdt=0,5 [Accessed 15/08/ 2020].

WHO. 2021. *World Malaria Report* [Online]. Available: https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2021 [Accessed 11/01 2022].

Wille, T., Thiermann, H. & Worek, F. 2011. In vitro kinetic interactions of DEET, pyridostigmine and organophosphorus pesticides with human cholinesterases. *Chemico-Biological Interactions,* 190**,** 79-83.

Willie, N., Mehlotra, R. K., Howes, R. E., Rakotomanga, T. A., Ramboarina, S., Ratsimbasoa, A. C. & Zimmerman, P. A. 2018. Insights into the performance of sd bioline malaria ag p.F/pan rapid diagnostic test and *Plasmodium falciparum* histidine-rich protein 2 gene variation in Madagascar. *The American Journal Of Tropical Medicine And Hygiene,* 98**,** 1683-1691.

Wilson, D. W., Langer, C., Goodman, C. D., McFadden, G. I. & Beeson, J. G. 2013. Defining the timing of action of antimalarial drugs against *Plasmodium falciparum*. *Antimicrobial Agents And Chemotherapy,* 57**,** 1455-1467.

Wilson, M. L. 2013. Laboratory diagnosis of malaria: conventional and rapid diagnostic methods. *Archives Of Pathology And Laboratory Medicine,* 137**,** 805-11.

Wogu, M. N. & Nduka, F. O. 2018. Evaluating malaria prevalence using clinical diagnosis compared with microscopy and rapid diagnostic tests in a tertiary healthcare facility in Rivers State, Nigeria. *Journal Of Tropical Medicine,* 2018**,** 1-4.

WorldPopulationReview. 2020. *Johannesburg population 2020* [Online]. Available: https://worldpopulationreview.com/world-cities/johannesburg-population/ [Accessed 30/04/ 2020].

Xu, P., Choo, Y.-M., De La Rosa, A. & Leal, W. S. 2014. Mosquito odorant receptor for DEET and methyl jasmonate. *Proceedings of the National Academy of Sciences,* 111**,** 16592-16597.

Yamamoto, S., Souares, A., Sié, A. & Sauerborn, R. 2010. Does recent contact with a health care provider make a difference in malaria knowledge? *Journal Of Tropical Pediatrics,* 56**,** 414-420.

Yang, G.-G., Kim, D., Pham, A. & Paul, C. J. 2018. A meta-regression analysis of the effectiveness of mosquito nets for malaria control: The value of long-lasting insecticide nets. *International Journal Of Environmental Research And Public Health,* 15**,** 546-557.

Yaya, S., Uthman, O. A., Amouzou, A. & Bishwajit, G. 2018. Mass media exposure and its impact on malaria prevention behaviour among adult women in sub-Saharan Africa: results from malaria indicator surveys. *Global Health Research And Policy,* 3**,** 1-9.

Yeung, S. 2018. Malaria—update on antimalarial resistance and treatment approaches. *The Pediatric Infectious Disease Journal,* 37**,** 367-369.

Zhang, Y., Xu, G., Zhang, S., Wang, D., Saravana Prabha, P. & Zuo, Z. 2018. Antitumor research on artemisinin and its bioactive derivatives. *Natural Products And Bioprospecting,* 8**,** 303-319.

Zhao, R., Wang, R., Zheng, L., Zhou, Y., Wang, L., Zhao, F., et al. 2019. Toxicity and repellency of two anthranilates against *Aedes albopictus Skuse* (Diptera: Culicidae). *Acta Tropica,* 200**,** 105171-105177.

Zinszer, K., Charland, K., Vahey, S., Jahagirdar, D., Rek, J. C., Arinaitwe, E., et al. 2019. The impact of multiple rounds of indoor residual spraying on malaria incidence and hemoglobin levels in a high-transmission setting. *The Journal Of Infectious Diseases,* 221**,** 304–312.

APPENDIX A

Approval to use to modify data collection instrument (Questionnaire).

9TH April,2019.

RE: REQUEST FOR PERMISSION TO USE SURVEY INSTRUMENT.

Dear Mr. Germain Gil Padonou,

My name is Mustapha Halidu Aliero, and I am a Pharmacology Masters student (MSc Med) by dissertation at the Faculty of Health Sciences, University of the Witwatersrand, South Africa. My research topic is titled: Knowledge, attitudes and perceptions on the management of Malaria and evaluation of efficacy of the available mosquito repellents in Johannesburg, South Africa. The project will be supervised by Professor Robyn Van Zyl and Professor Shelly Schmollgruber.

Sir, I am requesting your permission to give me access and to use your research questionnaire which you used for your research paper titled: knowledge- Attitudes-Practices about malaria among communities in Southern Benin. Published in International Journal of Public Health Science, Vol. 7, No. 3, On September,2018.

I will use this questionnaire only for my research project and the copyright statement will be included on all copies of the instrument.

If you agree and grant me permission to use the research instrument please indicate so by signing this letter and returning it to me together with the copy of the research instrument via this e-mail (1960843@students.wits.ac.za).

Alternatively, you may provide me a signed letter acknowledging that you grant me permission to use the study instrument and return it to me via the above e-mail address with a copy of the research instrument.

Thank you for your time and consideration in this matter.

Yours sincerely,

Dr. Mustapha Halidu Aliero,
(MBBS, Masters Student),
Department of Pharmacy and Pharmacology.
University of the Witwatersrand.
Johannesburg,
South Africa.
Approved by:

_ Germain Gil Padonou_____ __28/10/2019_____

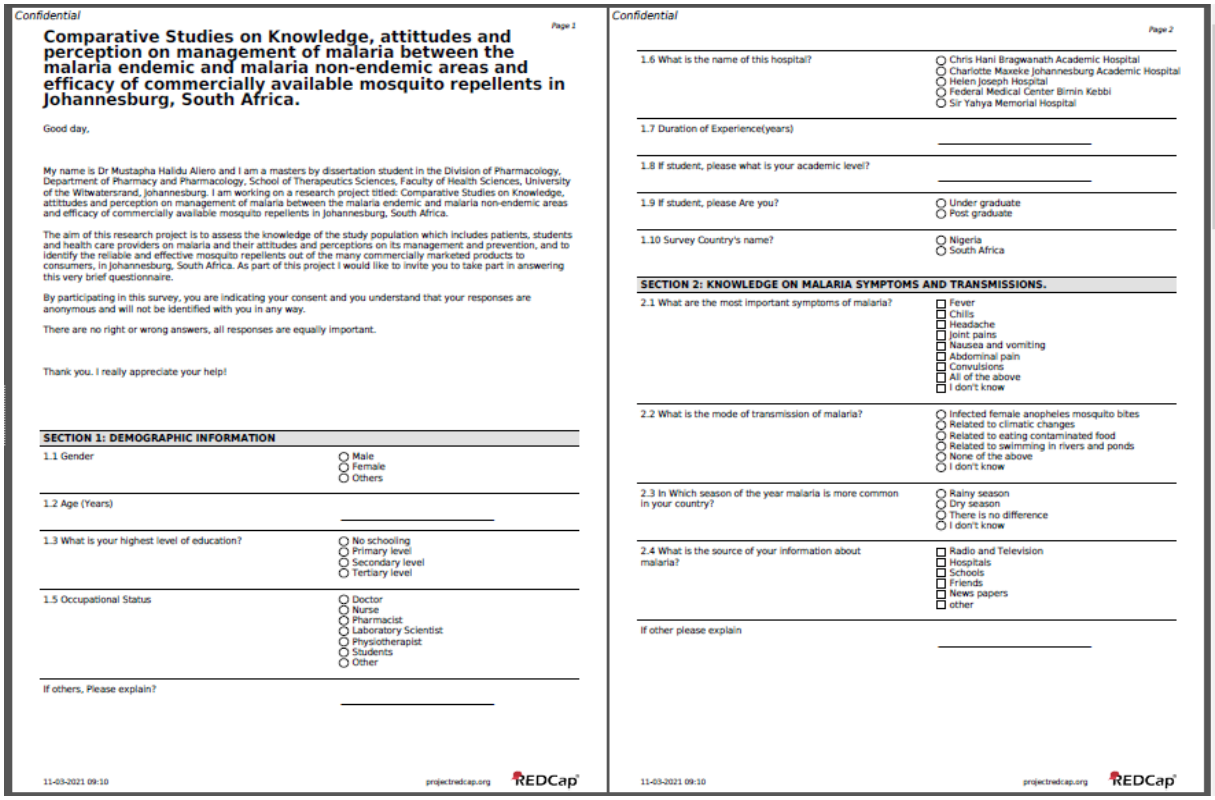
Date Signature

Enseignant-Chercheur PhD. MSc, DEA
Directeur du Centre de Recherche Entomologique de Cotonou
Entomologie Médicale et Vétérinaire
Environnement et Santé
Centre de Recherche Entomologique de Cotonou (Ministère de la Santé)
Faculté des Sciences et Techniques (Université d'Abomey -Calavi)
Tél : 00229 97289615 / 00229 64849595
République du Bénin

Centre de Recherche Entomologique de Cotonou * CREC * Le Directeur

APPENDIX B

Questionnaire



Confidential

Page 1

Comparative Studies on Knowledge, attittudes and perception on management of malaria between the malaria endemic and malaria non-endemic areas and efficacy of commercially available mosquito repellents in Johannesburg, South Africa.

Good day,

My name is Dr Mustapha Halidu Aliero and I am a masters by dissertation student in the Division of Pharmacology, Department of Pharmacy and Pharmacology, School of Therapeutics Sciences, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg. I am working on a research project titled: Comparative Studies on Knowledge, attittudes and perception on management of malaria between the malaria endemic and malaria non-endemic areas and efficacy of commercially available mosquito repellents in Johannesburg, South Africa.

The aim of this research project is to assess the knowledge of the study population which includes patients, students and health care providers on malaria and their attitudes and perceptions on its management and prevention, and to identify the reliable and effective mosquito repellents out of the many commercially marketed products to consumers, in Johannesburg, South Africa. As part of this project I would like to invite you to take part in answering this very brief questionnaire.

By participating in this survey, you are indicating your consent and you understand that your responses are anonymous and will not be identified with you in any way.

There are no right or wrong answers, all responses are equally important.

Thank you. I really appreciate your help!

SECTION 1: DEMOGRAPHIC INFORMATION

1.1 Gender
- ○ Male
- ○ Female
- ○ Others

1.2 Age (Years) _____

1.3 What is your highest level of education?
- ○ No schooling
- ○ Primary level
- ○ Secondary level
- ○ Tertiary level

1.5 Occupational Status
- ○ Doctor
- ○ Nurse
- ○ Pharmacist
- ○ Laboratory Scientist
- ○ Physiotherapist
- ○ Students
- ○ Other

If others, Please explain? _____

11-03-2021 09:10 projectredcap.org REDCap

Confidential

Page 2

1.6 What is the name of this hospital?
- ○ Chris Hani Bragwanath Academic Hospital
- ○ Charlotte Maxeke Johannesburg Academic Hospital
- ○ Helen Joseph Hospital
- ○ Federal Medical Center Birnin Kebbi
- ○ Sir Yahya Memorial Hospital

1.7 Duration of Experience(years) _____

1.8 If student, please what is your academic level? _____

1.9 If student, please Are you?
- ○ Under graduate
- ○ Post graduate

1.10 Survey Country's name?
- ○ Nigeria
- ○ South Africa

SECTION 2: KNOWLEDGE ON MALARIA SYMPTOMS AND TRANSMISSIONS.

2.1 What are the most important symptoms of malaria?
- ☐ Fever
- ☐ Chills
- ☐ Headache
- ☐ Joint pains
- ☐ Nausea and vomiting
- ☐ Abdominal pain
- ☐ Convulsions
- ☐ All of the above
- ☐ I don't know

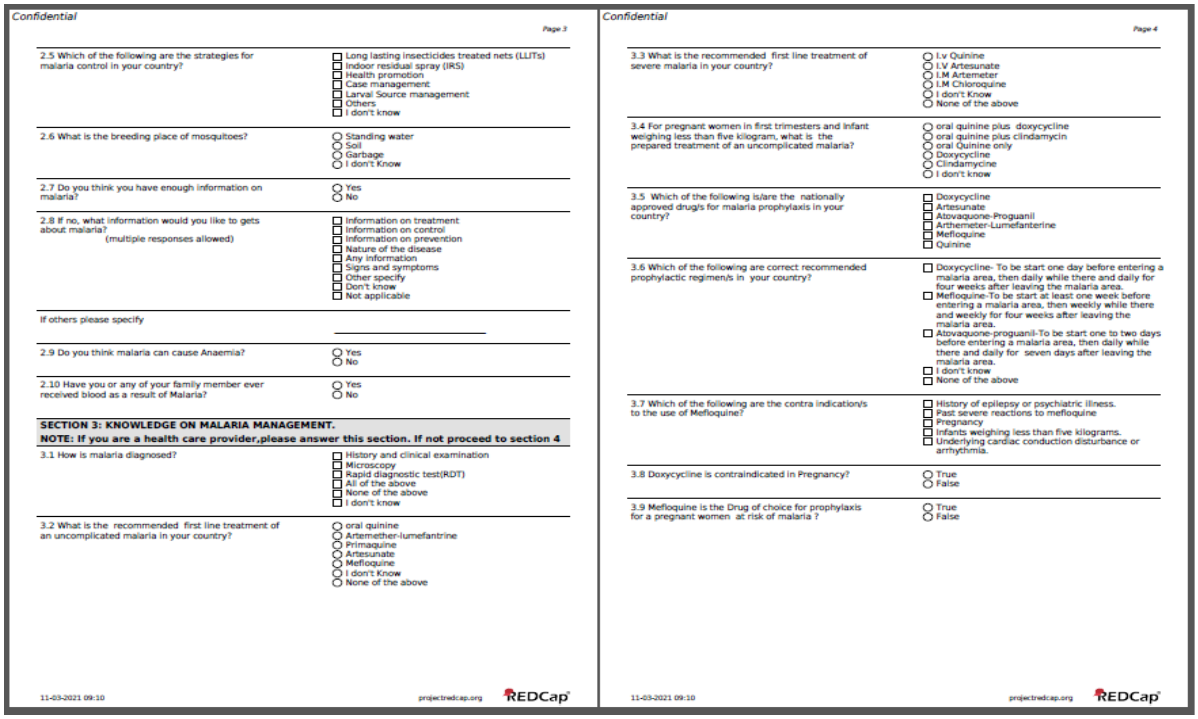
2.2 What is the mode of transmission of malaria?
- ○ Infected female anopheles mosquito bites
- ○ Related to climatic changes
- ○ Related to eating contaminated food
- ○ Related to swimming in rivers and ponds
- ○ None of the above
- ○ I don't know

2.3 In Which season of the year malaria is more common in your country?
- ○ Rainy season
- ○ Dry season
- ○ There is no difference
- ○ I don't know

2.4 What is the source of your information about malaria?
- ☐ Radio and Television
- ☐ Hospitals
- ☐ Schools
- ☐ Friends
- ☐ News papers
- ☐ other

If other please explain _____

11-03-2021 09:10 projectredcap.org REDCap



Confidential

Page 3

2.5 Which of the following are the strategies for malaria control in your country?
- ☐ Long lasting insecticides treated nets (LLITs)
- ☐ Indoor residual spray (IRS)
- ☐ Health promotion
- ☐ Case management
- ☐ Larval Source management
- ☐ Others
- ☐ I don't know

2.6 What is the breeding place of mosquitoes?
- ○ Standing water
- ○ Soil
- ○ Garbage
- ○ I don't Know

2.7 Do you think you have enough information on malaria?
- ○ Yes
- ○ No

2.8 If no, what information would you like to gets about malaria? (multiple responses allowed)
- ☐ Information on treatment
- ☐ Information on control
- ☐ Information on prevention
- ☐ Nature of the disease
- ☐ Any information
- ☐ Signs and symptoms
- ☐ Other specify
- ☐ Don't know
- ☐ Not applicable

If others please specify _____

2.9 Do you think malaria can cause Anaemia?
- ○ Yes
- ○ No

2.10 Have you or any of your family member ever received blood as a result of Malaria?
- ○ Yes
- ○ No

SECTION 3: KNOWLEDGE ON MALARIA MANAGEMENT.

NOTE: If you are a health care provider,please answer this section. If not proceed to section 4

3.1 How is malaria diagnosed?
- ☐ History and clinical examination
- ☐ Microscopy
- ☐ Rapid diagnostic test(RDT)
- ☐ All of the above
- ☐ None of the above
- ☐ I don't know

3.2 What is the recommended first line treatment of an uncomplicated malaria in your country?
- ○ oral quinine
- ○ Artemether-lumefantrine
- ○ Primaquine
- ○ Artesunate
- ○ Mefloquine
- ○ I don't Know
- ○ None of the above

11-03-2021 09:10 projectredcap.org REDCap

Confidential

Page 4

3.3 What is the recommended first line treatment of severe malaria in your country?
- ○ I.v Quinine
- ○ I.V Artesunate
- ○ I.M Artemeter
- ○ I.M Chloroquine
- ○ I don't Know
- ○ None of the above

3.4 For pregnant women in first trimesters and infant weighing less than five kilogram, what is the prepared treatment of an uncomplicated malaria?
- ○ oral quinine plus doxycycline
- ○ oral quinine plus clindamycin
- ○ oral Quinine only
- ○ Doxycycline
- ○ Clindamycine
- ○ I don't know

3.5 Which of the following is/are the nationally approved drug/s for malaria prophylaxis in your country?
- ☐ Doxycycline
- ☐ Artesunate
- ☐ Atovaquone-Proguanil
- ☐ Arthemeter-Lumefanterine
- ☐ Mefloquine
- ☐ Quinine

3.6 Which of the following are correct recommended prophylactic regimen/s in your country?
- ☐ Doxycycline- To be start one day before entering a malaria area, then daily while there and daily for four weeks after leaving the malaria area.
- ☐ Mefloquine-To be start at least one week before entering a malaria area, then weekly while there and weekly for four weeks after leaving the malaria area.
- ☐ Atovaquone-proguanil-To be start one to two days before entering a malaria area, then daily while there and daily for seven days after leaving the malaria area.
- ☐ I don't know
- ☐ None of the above

3.7 Which of the following are the contra indication/s to the use of Mefloquine?
- ☐ History of epilepsy or psychiatric illness.
- ☐ Past severe reactions to mefloquine
- ☐ Pregnancy
- ☐ Infants weighing less than five kilograms.
- ☐ Underlying cardiac conduction disturbance or arrhythmia.

3.8 Doxycycline is contraindicated in Pregnancy?
- ○ True
- ○ False

3.9 Mefloquine is the Drug of choice for prophylaxis for a pregnant women at risk of malaria ?
- ○ True
- ○ False

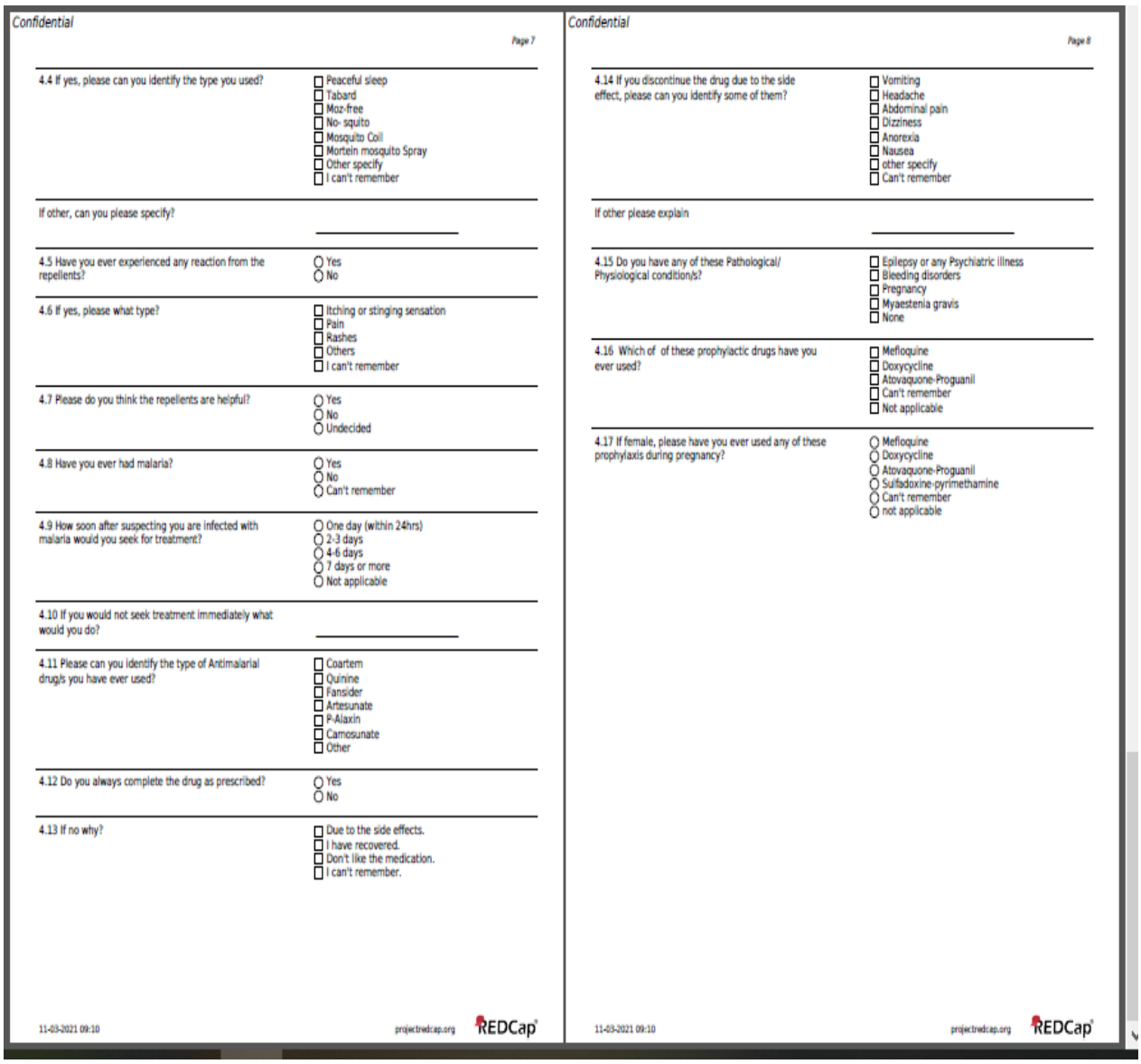
11-03-2021 09:10 projectredcap.org REDCap

3.10 Which of these dosages of Arthemeter 20mg+Lumefanterine 120mg is/are correct according to the patient weight?	☐ 5 -< 15 kg: One tablet stat, followed by one tablet after eight hours and then one tablets morning and evening on each of the following two days (total course = six tablets). ☐ 15-< 25 kg: Two tablets stat, followed by two tablets after eight hours and then two tablets morning and evening on each of the following two days (total course = 12 tablets) ☐ 25-< 35 kg: Three tablets stat, followed by three tablets after eight hours and then three tablets morning and evening on each of the following two days (total course = 18 tablets) ☐ 35-< 65 kg: Four tablets stat, followed by four tablets after eight hours and then four tablets morning and evening on each of the following two days (total course = 24 tablets). ☐ >65 kg: Dose as for those above35 kg. ☐ All of the above ☐ None of the above ☐ I can't remember
3.11 Which of these information do you think all patients diagnosed with malaria need to know?	☐ Takes all doses as directed, Coartem can be taken with fat containing food or drink ☐ Patient should take enough fluids and paracetamol for fever (not anti-inflammatory) ☐ Patient should expect improvement within 24-48hrs and return to the hospital if they remain unwell or their temperature doesn't subside after three days. ☐ Patient should return to the hospital if vomiting or deteriorating in anyway (e.g become sleepy, confused or jaundiced)
3.12 Which of these do you think is/ are the responsibilities of all health workers in both malaria endemic and non-endemic areas in order to achieve the ambitious targets of malaria elimination in South Africa (South Africans only)?	☐ Encouraging early treatment seeking within 24 to 48 hours. ☐ Maintaining a high index of suspicion to ensure prompt diagnostic testing of all patients with malaria symptoms who are resident in, or have recently travelled to, a malaria area. ☐ In those who test malaria positive, assess disease severity and start effective treatment immediately depending on disease severity. ☐ Notify each and every case (including all imported cases in non-endemic areas). ☐ Monitor adequacy of response to treatment.
3.13 Please do you always educate your patients about the information you selected in question 3.11?	○ Yes ○ No
3.14 Do you believe that almost all South Africans, including residents of seasonal malaria transmission areas , are non-immune and are therefore at increased risk of developing severe malaria (South Africans only).	○ Yes ○ No
3.15 Is Malaria a notifiable disease in your country?	○ Yes ○ No

3.16 From your clinical experience which of these antimalarial drugs do you think is the most effective in management of severe malaria?	○ Artesunate ○ Quinine ○ Artemether ○ Chloroquine ○ Equally effective ○ I don't know
3.17 Which province is the most affected in case of an odyssean malaria(infected mosquitoes being accidentally transported to non-endemic areas and transmit malaria) in South Africa? (South Africans only).	○ Eastern Cape ○ Free State ○ Gauteng ○ KwaZulu-Natal ○ Limpopo ○ Mpumalanga ○ Northern Cape ○ North West ○ Western Cape
3.18 What is the dose of an I.V Artesunate for a Patients weighing greater than 20kg?	_____
3.19 What is the dose of an I.V Artesunate for a patient weighing less than 20kg?	_____
3.20 The Goal of the National Malaria elimination program 2014-2020 in Nigeria is to reduce malaria burden to pre-elimination levels and bring malaria-related mortality to zero: has this being achieved ? (Nigerians only).	○ Yes ○ No
3.21 The recommended drug for the intermittent preventive therapy of malaria in pregnancy (IPTp) is? (Nigerians only).	○ Quinine ○ Sulfadoxine-Pyrimethermine ○ Arthemeter-lumefantrine ○ Oral Artesunate ○ Doxycycline ○ None of the above

SECTION 4: ATTITUDES AND PRACTICES REGARDING MALARIA

4.1 Do you think malaria is a preventable disease?	○ Yes ○ No
4.2 Which of these do you think will provide personal protection against malaria?	☐ Long lasting insecticide treated nets(LLINs) ☐ Mosquitoes repellents ☐ Clean environment ☐ Anti-malarial prophylaxis ☐ Seasonal Malaria Chemoprevention. ☐ Larval Source management ☐ All of the above ☐ Others specify ☐ I don't know
If other specify	_____
4.3 Have you ever used mosquito repellents?	○ Yes ○ No



Confidential

Page 7

4.4 If yes, please can you identify the type you used?
- ☐ Peaceful sleep
- ☐ Tabard
- ☐ Moz-free
- ☐ No- squito
- ☐ Mosquito Coil
- ☐ Mortein mosquito Spray
- ☐ Other specify
- ☐ I can't remember

If other, can you please specify?

4.5 Have you ever experienced any reaction from the repellents?
- ○ Yes
- ○ No

4.6 If yes, please what type?
- ☐ Itching or stinging sensation
- ☐ Pain
- ☐ Rashes
- ☐ Others
- ☐ I can't remember

4.7 Please do you think the repellents are helpful?
- ○ Yes
- ○ No
- ○ Undecided

4.8 Have you ever had malaria?
- ○ Yes
- ○ No
- ○ Can't remember

4.9 How soon after suspecting you are infected with malaria would you seek for treatment?
- ○ One day (within 24hrs)
- ○ 2-3 days
- ○ 4-6 days
- ○ 7 days or more
- ○ Not applicable

4.10 If you would not seek treatment immediately what would you do?

4.11 Please can you identify the type of Antimalarial drug/s you have ever used?
- ☐ Coartem
- ☐ Quinine
- ☐ Fansider
- ☐ Artesunate
- ☐ P-Alaxin
- ☐ Camosunate
- ☐ Other

4.12 Do you always complete the drug as prescribed?
- ○ Yes
- ○ No

4.13 If no why?
- ☐ Due to the side effects.
- ☐ I have recovered.
- ☐ Don't like the medication.
- ☐ I can't remember.

11-03-2021 09:10 projectredcap.org REDCap

Confidential

Page 8

4.14 If you discontinue the drug due to the side effect, please can you identify some of them?
- ☐ Vomiting
- ☐ Headache
- ☐ Abdominal pain
- ☐ Dizziness
- ☐ Anorexia
- ☐ Nausea
- ☐ other specify
- ☐ Can't remember

If other please explain

4.15 Do you have any of these Pathological/ Physiological condition/s?
- ☐ Epilepsy or any Psychiatric illness
- ☐ Bleeding disorders
- ☐ Pregnancy
- ☐ Myaestenia gravis
- ☐ None

4.16 Which of of these prophylactic drugs have you ever used?
- ☐ Mefloquine
- ☐ Doxycycline
- ☐ Atovaquone-Proguanil
- ☐ Can't remember
- ☐ Not applicable

4.17 If female, please have you ever used any of these prophylaxis during pregnancy?
- ○ Mefloquine
- ○ Doxycycline
- ○ Atovaquone-Proguanil
- ○ Sulfadoxine-pyrimethamine
- ○ Can't remember
- ○ not applicable

11-03-2021 09:10 projectredcap.org REDCap

APPENDIX C1

Consent form.

Consent form

1) I have been given Participant Information Sheet which explains the nature and all the processes involved in this study.
2) I was given enough time to read it and I understood what my participation means in this study.
3) I was given enough time to ask questions and I am satisfied with all the responses giving to me.
4) I fully understand why this study is been conducted and the expected outcomes.
5) I fully understand that I will not receive any immediate benefit for participation in this study, also my participation will not cost me anything except the few minutes I will spend in completing the study Questionnaire.
6) I understand that even if I initially consented to participate, I may choose not answer any question and I can withdraw without given any reason. The initial data I supplied can only be used with my permission otherwise it will be destroyed.
7) I understand I can contact the investigator, his supervisor or Ethics committee through the contact details supplied below if I have any concerned about this study.

Principal investigator: Halidu Mustapha Aliero, +27 84 7160 321, 1966648@students.wits.ac.za

Supervisor: Professor Robyn van Zyl, +27 83 313 022, Robyn.VanZyl@wits.ac.za.

Ethics Committee: Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za. Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za.

Participant Signature or mark: _____
Witnessed by:
Name of Witness: _____
Signature: _____
Date: _____

APPENDIX C2

Participant information Sheet.

School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

Faculty of Health Sciences · Private Bag 3, Wits, 2050, South Africa
Tel: +27 11 717 2542 · E-mail: Robyn.vanZyl@wits.ac.za · www.wits.ac.za

WITS UNIVERSITY

Monday, February 21, 2022

Dear Potential Participant,

My name is Dr Mustapha Halidu Allero and I am a masters by dissertation student in the Division of Pharmacology, Department of Pharmacy and Pharmacology, School of Therapeutics Sciences, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg. I am working on a research project titled: Malaria related knowledge and prevention practices: A comparative study between South Africa and Nigeria; and efficacy of commercially- available mosquito repellants.The aim of this research project is to assess the knowledge of the study population which includes patients, students and health care providers on malaria and their attitudes and perceptions on its management and prevention in Birnin Kebbi Metropolis, Nigeria and Johannesburg, South Africa, and to identify the reliable and effective mosquito repellents out of the many commercially marketed products to consumers in Johannesburg, South Africa. As part of this project I would like to invite you to take part in answering a questionnaire. The study areas for this study include: Federal Medical Centre Birnin Kebbi, Sir Yahya Memorial hospital, Charlotte Maxeke Johannesburg Academic Hospital, Chris Hani Bragwanath Hospital and Helen Joseph Hospital. The questionnaire is very brief and will take an approximate of 20 minutes or less. The questionnaire can be administered through email or paper and pen depending on your preference.

Participants will be asked about their knowledge, attitudes and perceptions on malaria and its management according to the Nigerian and south African malaria treatments guidelines. There is not any known or anticipated risk to participation in this study and you will not receive any direct benefit from participating in this study. Participation is voluntary and there are no disadvantages or penalties for not participating. You may withdraw at any time or not answer any question if you do not want to. The survey will be completely confidential and anonymous as I will not be asking for your name or any identifying information, and the information you give to me will be held securely and not disclosed to anyone else. The data from this questionnaire will be aggregated so that no single response will be identified.

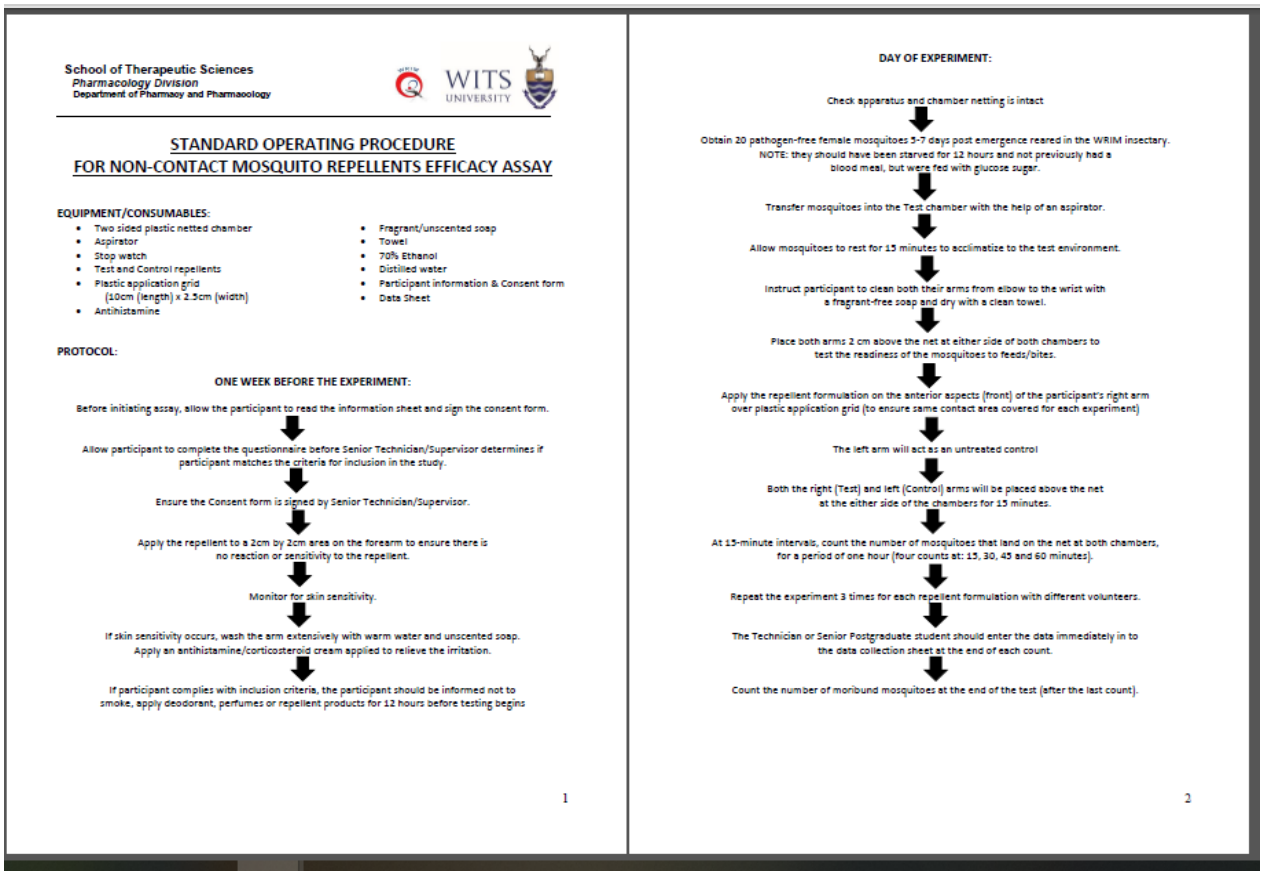
If you have any questions afterwards about this research, feel free to contact me on the details listed below. This study will be written up as a thesis which will be available online through the university library website. It may also be published in scientific journals and presented at academic meetings, but your identity will not be revealed. If you wish to receive a summary of this report, I will be happy to send it to you upon request. If you have any queries, concerns, or complaints regarding the ethical procedures of this study, you are welcome to contact the University Human Research Ethics Committee (medical), telephone +27(0)11 717 1408, email: hreo- medical.research@wits.ac.za/; Shaun.Schoeman@wits.ac.za

Yours sincerely,

Dr Mustapha Halidu Allero, 1966648@students.wits.ac.za, 084 716 0321 (Student)
Professor Robyn van Zyl, Robyn.VanZyl@wits.ac.za, 083 312 0228 (Supervisor)
Professor Shelley Schmoilgruber, Shelley. Schmoilgruber@wits.ac.za (Supervisor).

APPENDIX D

SOPs and Consent form for efficacy assays



School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

STANDARD OPERATING PROCEDURE
FOR NON-CONTACT MOSQUITO REPELLENTS EFFICACY ASSAY

EQUIPMENT/CONSUMABLES:

- Two sided plastic netted chamber
- Aspirator
- Stop watch
- Test and Control repellents
- Plastic application grid (10cm (length) x 2.5cm (width)
- Antihistamine
- Fragrant/unscented soap
- Towel
- 70% Ethanol
- Distilled water
- Participant information & Consent form
- Data Sheet

PROTOCOL:

ONE WEEK BEFORE THE EXPERIMENT:

Before initiating assay, allow the participant to read the information sheet and sign the consent form.

↓

Allow participant to complete the questionnaire before Senior Technician/Supervisor determines if participant matches the criteria for inclusion in the study.

↓

Ensure the Consent form is signed by Senior Technician/Supervisor.

↓

Apply the repellent to a 2cm by 2cm area on the forearm to ensure there is no reaction or sensitivity to the repellent.

↓

Monitor for skin sensitivity.

↓

If skin sensitivity occurs, wash the arm extensively with warm water and unscented soap. Apply an antihistamine/corticosteroid cream applied to relieve the irritation.

↓

If participant complies with inclusion criteria, the participant should be informed not to smoke, apply deodorant, perfumes or repellent products for 12 hours before testing begins

1

DAY OF EXPERIMENT:

Check apparatus and chamber netting is intact

↓

Obtain 20 pathogen-free female mosquitoes 5-7 days post emergence reared in the WRIM insectary. NOTE: they should have been starved for 12 hours and not previously had a blood meal, but were fed with glucose sugar.

↓

Transfer mosquitoes into the Test chamber with the help of an aspirator.

↓

Allow mosquitoes to rest for 15 minutes to acclimatize to the test environment.

↓

Instruct participant to clean both their arms from elbow to the wrist with a fragrant-free soap and dry with a clean towel.

↓

Place both arms 2 cm above the net at either side of both chambers to test the readiness of the mosquitoes to feeds/bites.

↓

Apply the repellent formulation on the anterior aspects (front) of the participant's right arm over plastic application grid (to ensure same contact area covered for each experiment)

↓

The left arm will act as an untreated control

↓

Both the right (Test) and left (Control) arms will be placed above the net at the either side of the chambers for 15 minutes.

↓

At 15-minute intervals, count the number of mosquitoes that land on the net at both chambers, for a period of one hour (four counts at: 15, 30, 45 and 60 minutes).

↓

Repeat the experiment 3 times for each repellent formulation with different volunteers.

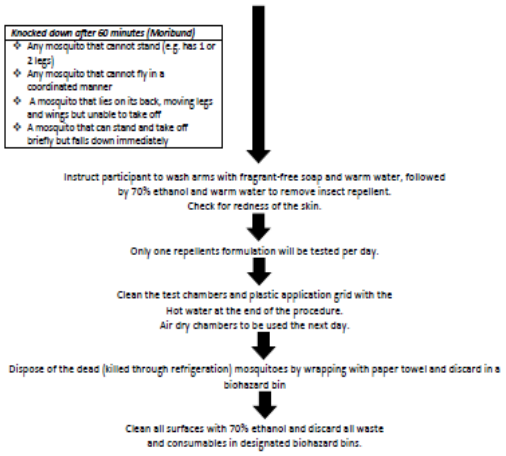
↓

The Technician or Senior Postgraduate student should enter the data immediately in to the data collection sheet at the end of each count.

↓

Count the number of moribund mosquitoes at the end of the test (after the last count).

2



School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

Study title: *The Mosquito Repellent and Insecticidal Properties of Novel Synthetic and Natural Compounds.*

Dear Potential Participant

My name is Professor Robyn van Zyl, Pharmacology Research Co-ordinator of the WITS Research Institute of Malaria (WRIM) in the Faculty of Health Sciences at the University of the Witwatersrand, where we are undertaking research on the efficacy of insect/mosquito repellents and their insecticidal properties.

In this study, we want to learn more about what attracts mosquitoes to certain people and not others. In addition, there are numerous products commercially available online or from stores or street vendors, with the majority them not been approved by the South African Standards Bureau or validated scientifically. Effective and safe malaria prophylaxis is critical to prevent malaria infections. The efficacy of the products varying from physical barriers, chemicals (traditional or synthetic origin) or electronic devices lure the community to believe they are being adequately protected, but if not applied or used correctly, no protection will be offered. As such this study will investigate the attraction of the mosquito to a host and then the test repellent (natural/synthetic compound or electronic device) will be applied and compared to the standard repellent (DEET). The 'arm-on-cage' methodology will be used such that the volunteer is not bitten by the mosquito, but their arms will be used to attract the mosquito to determine attraction or repellent rate at 15 minute intervals over an hour. Each volunteer will act as their own control where one arm will be repellent-free and the other arm will have the repellent applied. By participating in this study, you will assist us in gaining further knowledge as to which natural and synthetic compound or electronic device has the potential to effectively prevent mosquito bites in our population and reduce the risk of malaria infections. As such, we invite you to take part in this research study.

The design of the experiments and apparatus to be used will prevent you from being bitten by the mosquitoes, which will be pathogen-free to prevent infections. To monitor for any possible sensitivities to the commercially available or natural/synthetic products, a spot sensitivity test will be done one week before the repellent is to be applied to the lower half of your arm. There is no other known or anticipated risks to participation in this study.

You will not receive any direct benefit from participating in this study, but the outcome for your own data and overall outcome of the study will be made available to you. Participation is voluntary and there are no disadvantages or penalties for not participating. You may withdraw at any time or not answer any question if you do not want to. The survey will be completely confidential and the information you give to me will be held securely and not publically disclosed. The data from the study will be aggregated so that no single response will be identified.

If you have any questions afterwards about this research, feel free to contact me on the details listed below. This study will be written up as a publication or used in postgraduate student outputs, which will be available online through the WITS University library website. It will be presented at academic meetings, but your identity will not be revealed. If you wish to receive a summary of this report, I will be happy to send it to you upon request.

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg ("Committee"). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for reading this Study Information Sheet.

Yours sincerely,

Professor Robyn van Zyl,
Robyn.VanZyl@wits.ac.za,
011-717-2271
083 312 0228

School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

PARTICIPANT CONSENT SHEET

Study title: *The Mosquito Repellent and Insecticidal Properties of Novel Synthetic and Natural Compounds.*

1. I have been given a Participant Information Sheet which explains the nature and processes involved in this study, which is attached hereto;
2. I was given time to read it, or had it read to me, in the language I best understand;
3. I was given time to ask any questions I wanted to and found any answers given to me to be reasonable and satisfactory;
4. I believe I fully understand why the study is being conducted and what the intended outcomes will be;
5. I understand that there will be no immediate benefit to me, should I agree to participate, nor will I receive any payment; conversely, participation will not cost me anything but my time;
6. I understand that, even if I initially consent to take part in the study, I may subsequently withdraw at any time and would not be required to give any reasons; if that happened, any data collected about me for the purposes of the study would immediately be destroyed, unless I give consent for it to be retained
7. I have been given a range of contact details, listed below. If I require further information or become concerned about any aspect of this study I am free to speak to any of these contacts.

Contact details:
Professor Robyn van Zyl, Principal Investigator, telephone no. 011-717-2271, or by e-mail at Robyn.VanZyl@wits.ac.za,

Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za.
Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

Name of Participant: _____

Date: _____

Place: _____

Signature or mark _____

Witnessed by:

Name of Witness: _____

Signature: _____

Date: _____

School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

Pharmacology Division / WRIM
Self-administered Mosquito Repell Volunteer Questionairre

Surname			
First name			
Age			
Assigned Participant #			
Contact information if requiring outcome of study: email:			
To assess if you meet all the inclusion and exclusion criteria for participating in this study, please complete the following two sheets each time you participate.			
Participant #			
Test date			
Are you in good health today?	Y	N	
Eaten in the last 4 hours?	Y	N	
Previous allergy to insect repellent?	Y	N	
If so, what product?			
Do you suffer from any of the following?			
Skin conditions?	Y	N	
Lung disorders?	Y	N	
Do you have a Pace-maker*?	Y	N	
Other health information to share?	Y	N	
Is the Consent form signed?	Y	N	
Participant signature:			
Approved to Participate:	Y	N	
PI/ Senior Technician signature			

To note:

APPENDIX E

Repellent efficacy assays data collection sheet.

School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

REPELLENT EFFICACY ASSAY DATA COLLECTION SHEET :

EFFICACY ASSAY Code:
PRODUCT NAME:
PRODUCT CONCENTRATION:

MOSQUITO SPECIE:
SOURCE:
NAME OF MOSQUITOES SUPPLIER:
ASSAY ROOM TEMPERATURE:
HOURS OF STABBING:
AGE IN DAYS:

ASSAY NUMBER ONE.

DATE OF AN ASSAY: Age=
Time of the day: Gender=
Number of mosquitoes on the treated Arm net at 15 minutes:
Number of mosquitoes on the untreated Arm net at 15 minutes:
Number of the mosquitoes in the treated arm chamber at 15 minutes:
Number of the mosquitoes in the untreated arm chamber at 15 minutes:
Number of the mosquitoes in the middle chamber at 15 minutes:
Number of an Undecided mosquitoes in both chambers at 15minutes:

Number of mosquitoes on the treated Arm net at 30 minutes:
Number of mosquitoes on the untreated Arm net at 30 minutes:
Number of the mosquitoes in the treated arm chamber at 30 minutes:
Number of the mosquitoes in the untreated arm chamber at 30 minutes:
Number of the mosquitoes in the middle chamber at 30 minutes:
Number of an Undecided mosquitoes in both chambers at 30 minutes:

Number of mosquitoes on the treated Arm net at 45 minutes:
Number of mosquitoes on the untreated Arm net at 45 minutes:
Number of the mosquitoes in the treated arm chamber at 45 minutes:
Number of the mosquitoes in the untreated arm chamber at 45 minutes:
Number of the mosquitoes in the middle chamber at 45 minutes:
Number of an Undecided mosquitoes in both chambers at 45 minutes:

Number of mosquitoes on the treated Arm net at 60 minutes:
Number of mosquitoes on the untreated Arm net at 60 minutes:
Number of the mosquitoes in the treated arm chamber at 60 minutes:
Number of the mosquitoes in the untreated arm chamber at 60 minutes:
Number of the mosquitoes in the middle chamber at 60 minutes:
Number of an Undecided mosquitoes in both chambers at 60 minutes:
Number of Moribund Mosquitoes:

Student signature:

Technician signature:

Check: Volunteer has read the information sheet and signed the consent form: Yes | No
File signed consent form in Volunteer folder.

ASSAY NUMBER TWO.

DATE OF AN ASSAY: Age=
Time of the day: Gender
Number of mosquitoes on the treated Arm net at 15 minutes:
Number of mosquitoes on the untreated Arm net at 15 minutes:
Number of the mosquitoes in the treated arm chamber at 15 minutes:
Number of the mosquitoes in the untreated arm chamber at 15 minutes:
Number of the mosquitoes in the middle chamber at 15 minutes:
Number of an Undecided mosquitoes in both chambers at 15minutes:

Number of mosquitoes on the treated Arm net at 30 minutes:
Number of mosquitoes on the untreated Arm net at 30 minutes:
Number of the mosquitoes in the treated arm chamber at 30 minutes:
Number of the mosquitoes in the untreated arm chamber at 30 minutes:
Number of the mosquitoes in the middle chamber at 30 minutes:
Number of an Undecided mosquitoes in both chambers at 30 minutes:

Number of mosquitoes on the treated Arm net at 45 minutes:
Number of mosquitoes on the untreated Arm net at 45 minutes:
Number of the mosquitoes in the treated arm chamber at 45 minutes:
Number of the mosquitoes in the untreated arm chamber at 45 minutes:
Number of the mosquitoes in the middle chamber at 45 minutes:
Number of an Undecided mosquitoes in both chambers at 45 minutes:

Number of mosquitoes on the treated Arm net at 60 minutes:
Number of mosquitoes on the untreated Arm net at 60 minutes:
Number of the mosquitoes in the treated arm chamber at 60 minutes:
Number of the mosquitoes in the untreated arm chamber at 60 minutes:

Number of the mosquitoes in the untreated arm chamber at 60 minutes:

Number of the mosquitoes in the middle chamber at 60 minutes:

Number of an Undecided mosquitoes in both chambers at 60 minutes:

Number of Moribund Mosquitoes:

Student signature:

Technician signature:

Check: Volunteer has read the information sheet and signed the consent form: **Yes** | **No**
File signed consent form in Volunteer folder

FINAL ANALYSIS OF EFFICACY OF:

EFFICACY ASSAY Code:

PRODUCT NAME:

PRODUCT CONCENTRATION:

Average number of mosquitoes on the treated Arm= Total number of mosquitoes counted for all the test = Number of the test (4).

Attraction rate (%) = Average number of mosquitoes on the treated Arm = Total number of mosquitoes used (20)

$$\%\text{Responding} = \frac{Nc + Nt}{20} =$$

$$\text{Spatial activity index (SAI)} = \frac{(Nc - Nt)}{(Nc + Nt)} \times \%\text{Responding} =$$

APPENDIX F

Protocol assessment committee and change of title approval letters.

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

27 August 2019
Person No: 1966648
PAG

Dr MA Halidu
Federal University
Kebbi
1157
Nigeria

Dear Dr Mustapha Halidu

Master of Science in Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *Knowledge, attitudes and perceptions on the management of Malaria and efficacy of the commercially available mosquitoes repellents in Johannesburg, South Africa* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

03 January 2022
Person No: 1966648
TAA

Dr MA Halidu
Federal University
Kebbi
1157
Nigeria

Dear Dr Mustapha Halidu

Master of Science in Medicine: Change of title of research

I am pleased to inform you that the following change in the title of your Dissertation for the degree of **Master of Science in Medicine** has been approved:

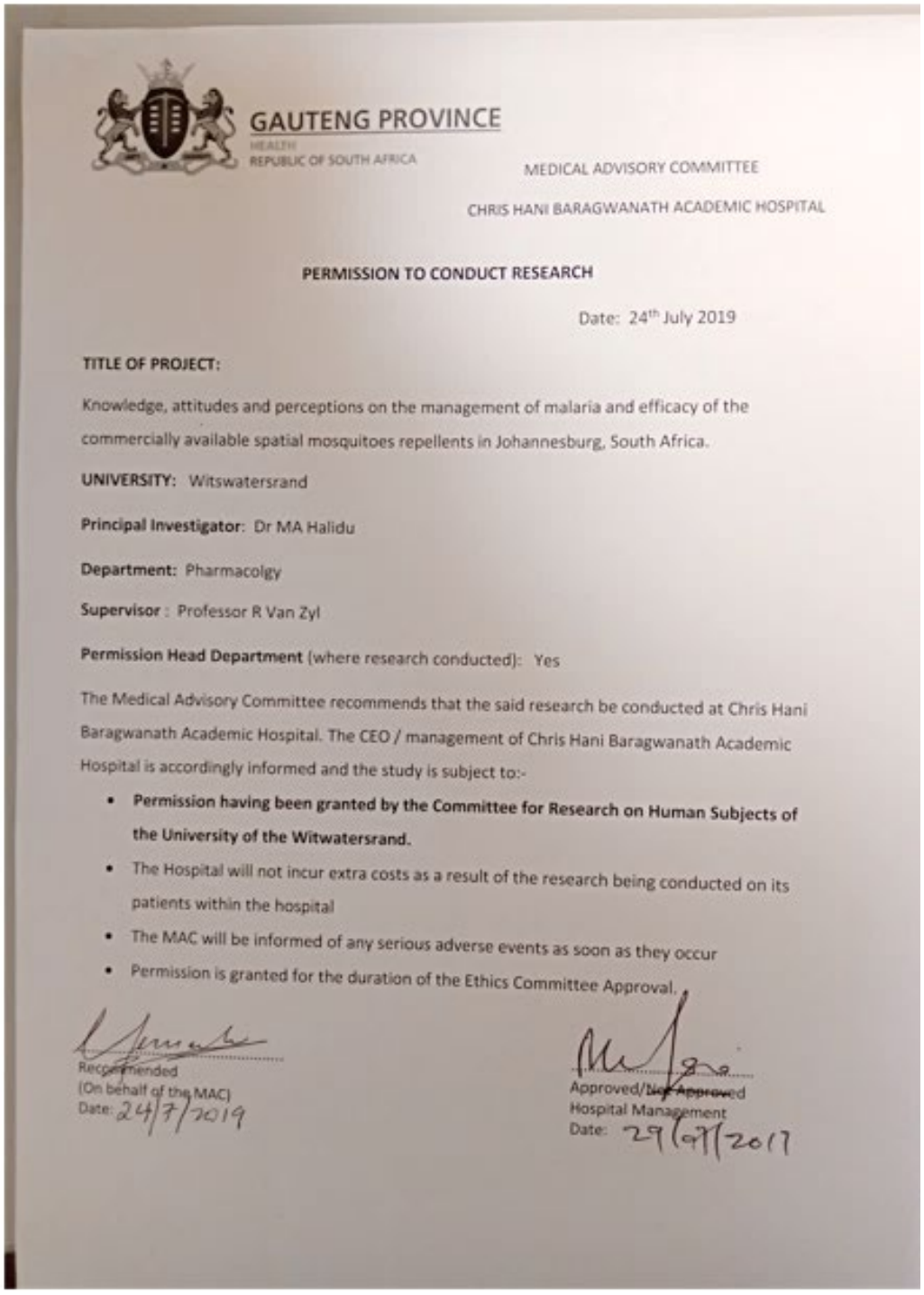
From:	**Knowledge, attitudes and perceptions on the management of Malaria and efficacy of the commercially available mosquitoes repellents in Johannesburg, South Africa**
To:	**Malaria related knowledge and prevention practices: A comparative study between South Africa and Nigeria; and efficacy of commercially available mosquito repellents.**

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

APPENDIX G

Chris Hani Baragwanath Academic Hospital CEO's approval letter.



GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 24th July 2019

TITLE OF PROJECT:

Knowledge, attitudes and perceptions on the management of malaria and efficacy of the commercially available spatial mosquitoes repellents in Johannesburg, South Africa.

UNIVERSITY: Witswatersrand

Principal Investigator: Dr MA Halidu

Department: Pharmacolgy

Supervisor : Professor R Van Zyl

Permission Head Department (where research conducted): Yes

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Academic Hospital. The CEO / management of Chris Hani Baragwanath Academic Hospital is accordingly informed and the study is subject to:-

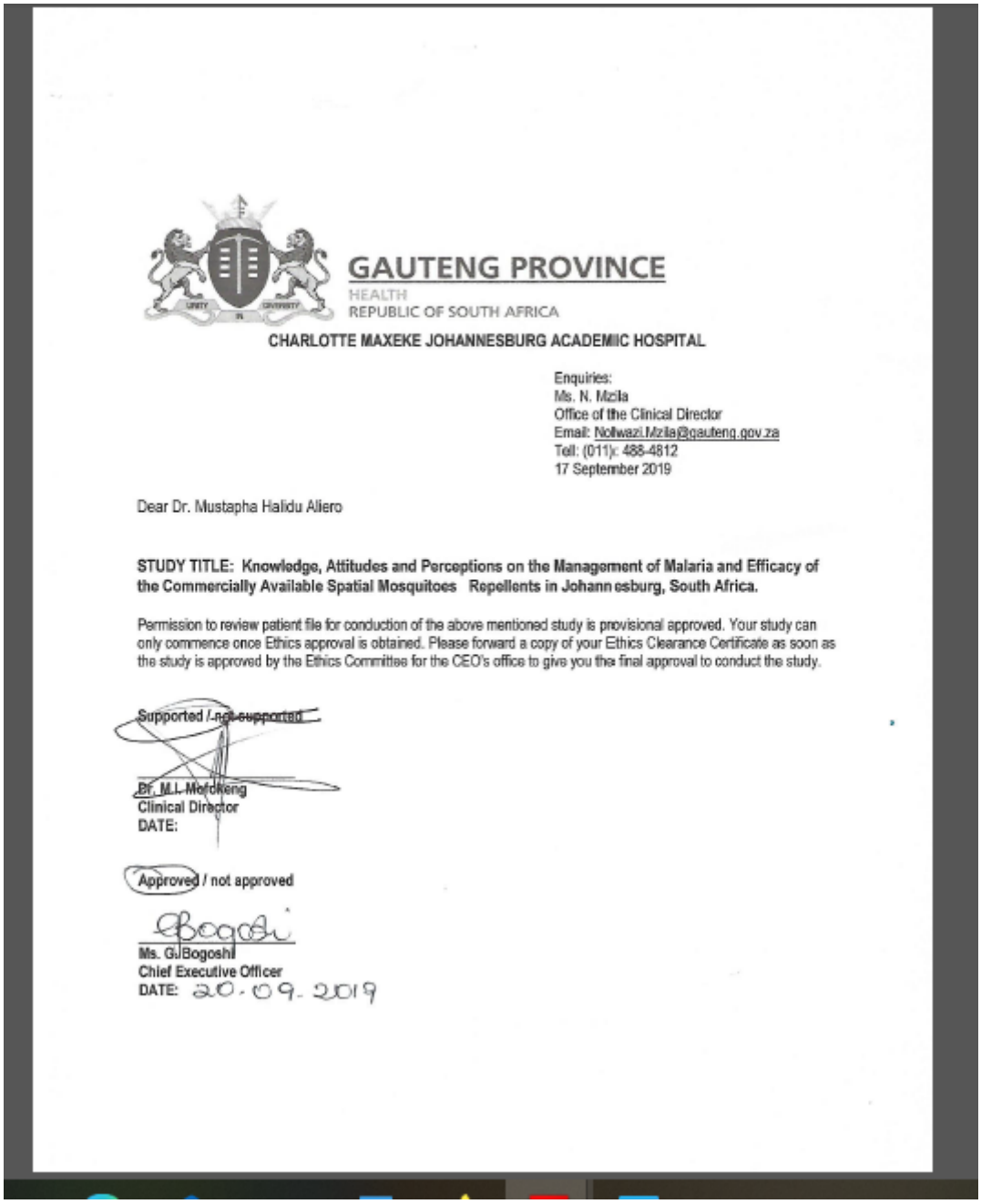
- **Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.**
- The Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- The MAC will be informed of any serious adverse events as soon as they occur
- Permission is granted for the duration of the Ethics Committee Approval.

Recommended
(On behalf of the MAC)
Date: 24/7/2019

Approved/~~Not Approved~~
Hospital Management
Date: 29/07/2019

APPENDIX H

Charlotte Maxeke Johannesburg Academic Hospital CEO's approval letter.



GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Enquiries:
Ms. N. Mzila
Office of the Clinical Director
Email: Nollwazi.Mzila@gauteng.gov.za
Tell: (011)\: 488-4812
17 September 2019

Dear Dr. Mustapha Halidu Allero

STUDY TITLE: Knowledge, Attitudes and Perceptions on the Management of Malaria and Efficacy of the Commercially Available Spatial Mosquitoes Repellents in Johannesburg, South Africa.

Permission to review patient file for conduction of the above mentioned study is provisional approved. Your study can only commence once Ethics approval is obtained. Please forward a copy of your Ethics Clearance Certificate as soon as the study is approved by the Ethics Committee for the CEO's office to give you the final approval to conduct the study.

Supported / ~~not supported~~

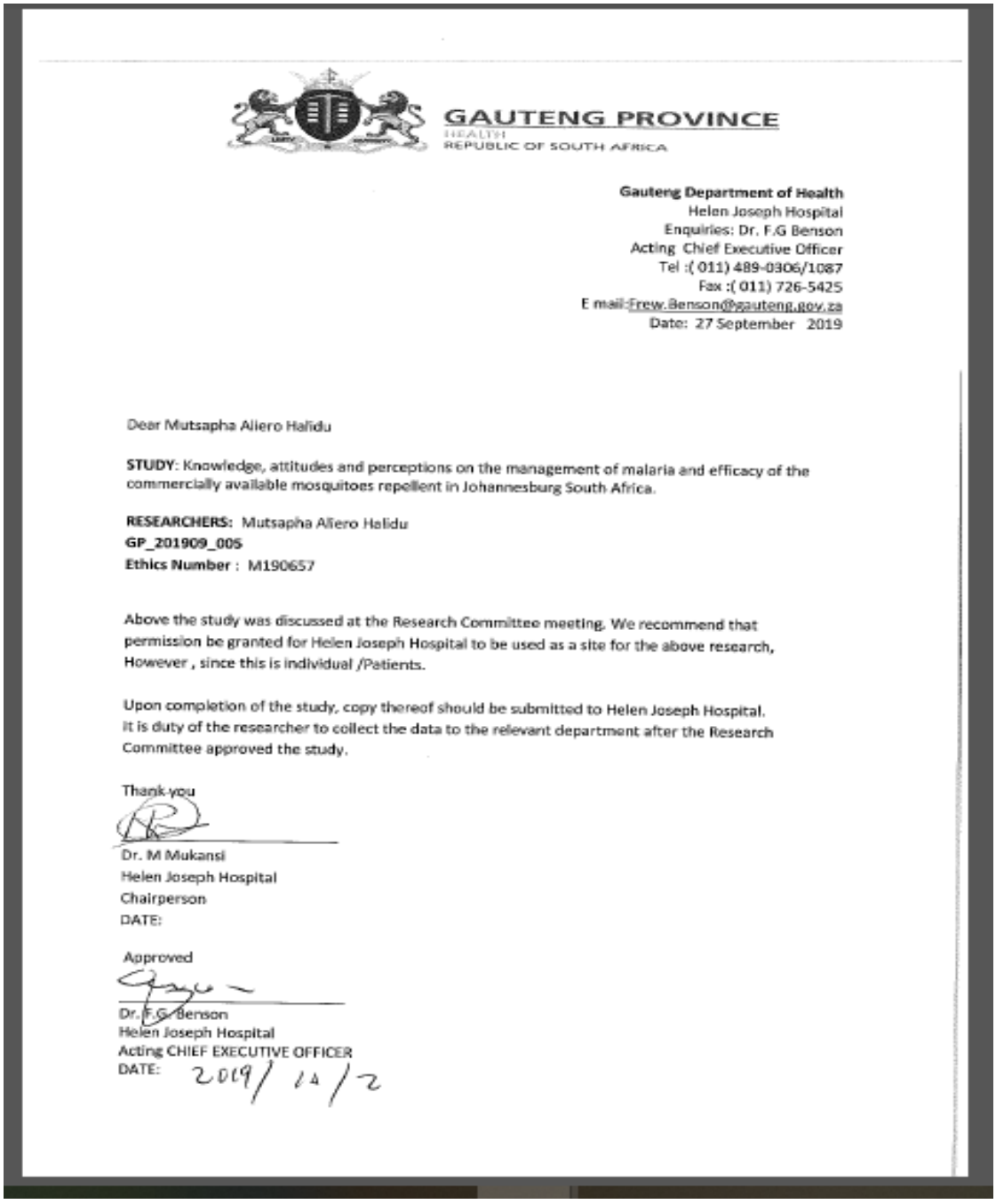
Dr. M.I. Motokeng
Clinical Director
DATE:

Approved / not approved

Ms. G. Bogoshi
Chief Executive Officer
DATE: 20-09-2019

APPENDIX I

Helen Joseph hospital CEO's approval letter.



GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

Gauteng Department of Health
Helen Joseph Hospital
Enquiries: Dr. F.G Benson
Acting Chief Executive Officer
Tel :(011) 489-0306/1087
Fax :(011) 726-5425
E mail:Frew.Benson@gauteng.gov.za
Date: 27 September 2019

Dear Mutsapha Aliero Halidu

STUDY: Knowledge, attitudes and perceptions on the management of malaria and efficacy of the commercially available mosquitoes repellent in Johannesburg South Africa.

RESEARCHERS: Mutsapha Aliero Halidu
GP_201909_005
Ethics Number : M190657

Above the study was discussed at the Research Committee meeting. We recommend that permission be granted for Helen Joseph Hospital to be used as a site for the above research, However , since this is individual /Patients.

Upon completion of the study, copy thereof should be submitted to Helen Joseph Hospital. It is duty of the researcher to collect the data to the relevant department after the Research Committee approved the study.

Thank you

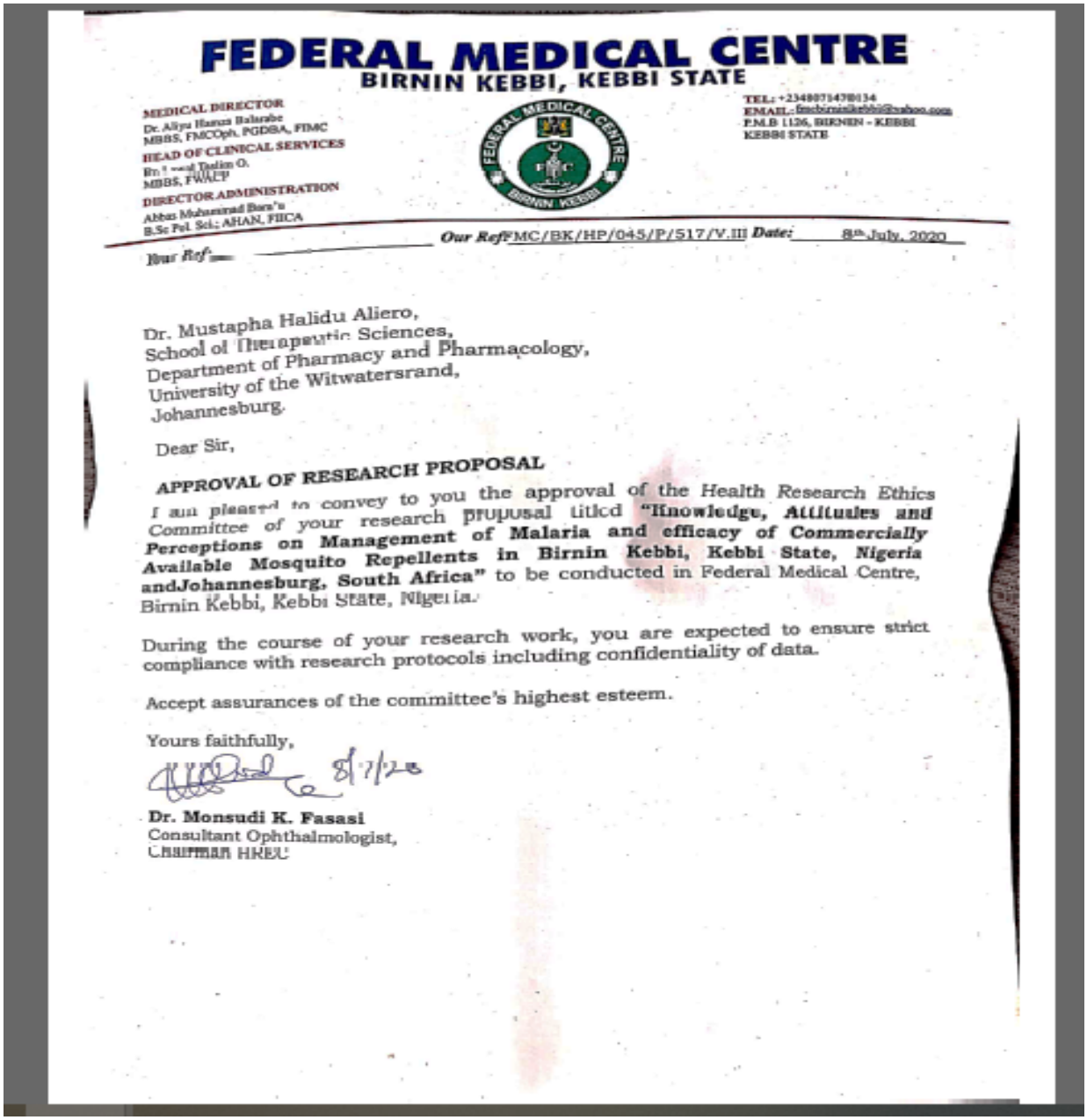
Dr. M Mukansi
Helen Joseph Hospital
Chairperson
DATE:

Approved

Dr. F.G Benson
Helen Joseph Hospital
Acting CHIEF EXECUTIVE OFFICER
DATE: 2019/ 10 /2

APPENDIX J

Federal Medical Centre Birnin Kebbi HREC approval letter.



FEDERAL MEDICAL CENTRE
BIRNIN KEBBI, KEBBI STATE

MEDICAL DIRECTOR
Dr. Aliyu Hamza Balarabe
MBBS, FMCOph, PGDBA, FIMC
HEAD OF CLINICAL SERVICES
Bn [illegible] Ibrahim O.
MBBS, FWACP
DIRECTOR ADMINISTRATION
Alhaji Muhammad Bara'u
B.Sc Pol. Sci.; AHAN, FIICA

TEL: +2348071478134
EMAIL: fmcbirninkebbi@yahoo.com
P.M.B 1126, BIRNIN - KEBBI
KEBBI STATE

Your Ref: _____ Our Ref FMC/BK/HP/045/P/517/V.III Date: 8th July, 2020

Dr. Mustapha Halidu Aliero,
School of Therapeutic Sciences,
Department of Pharmacy and Pharmacology,
University of the Witwatersrand,
Johannesburg.

Dear Sir,

APPROVAL OF RESEARCH PROPOSAL

I am pleased to convey to you the approval of the Health Research Ethics Committee of your research proposal titled **"Knowledge, Attitudes and Perceptions on Management of Malaria and efficacy of Commercially Available Mosquito Repellents in Birnin Kebbi, Kebbi State, Nigeria andJohannesburg, South Africa"** to be conducted in Federal Medical Centre, Birnin Kebbi, Kebbi State, Nigeria.

During the course of your research work, you are expected to ensure strict compliance with research protocols including confidentiality of data.

Accept assurances of the committee's highest esteem.

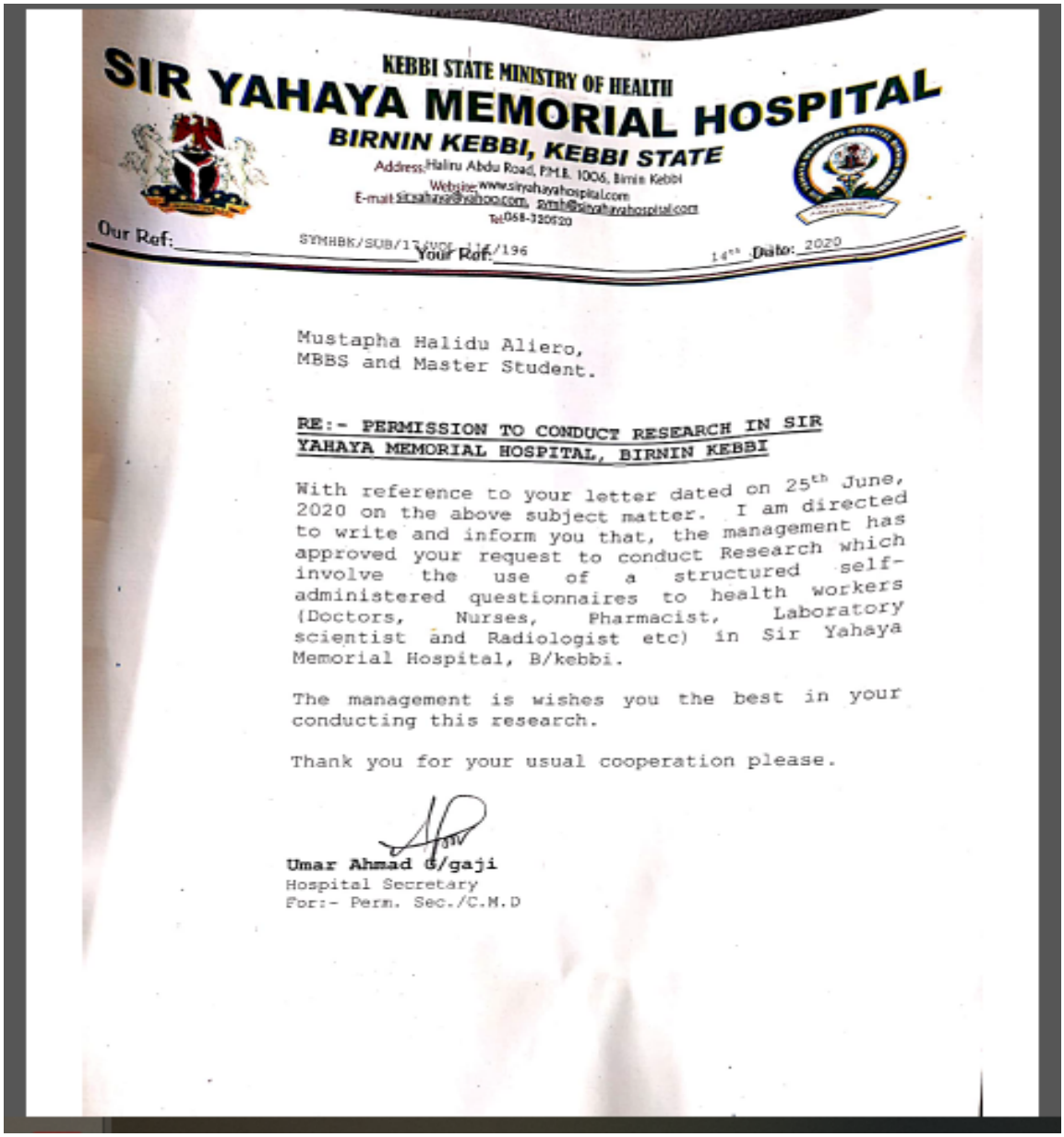
Yours faithfully,

8/7/20

Dr. Monsudi K. Fasasi
Consultant Ophthalmologist,
Chairman HREC

APPENDIX K

Sir Yahaya Memorial Hospital CEO's approval letter.



KEBBI STATE MINISTRY OF HEALTH

SIR YAHAYA MEMORIAL HOSPITAL

BIRNIN KEBBI, KEBBI STATE

Address: Haliru Abdu Road, P.M.B. 1006, Birnin Kebbi
Website: www.siryahayahospital.com
E-mail: siryahaya@yahoo.com, ymh@siryahayahospital.com
Tel: 068-320620

Our Ref: SYMHBK/SUB/17/VOL. III/196 Your Ref: 14th Date: 2020

Mustapha Halidu Aliero,
MBBS and Master Student.

RE:- PERMISSION TO CONDUCT RESEARCH IN SIR YAHAYA MEMORIAL HOSPITAL, BIRNIN KEBBI

With reference to your letter dated on 25th June, 2020 on the above subject matter. I am directed to write and inform you that, the management has approved your request to conduct Research which involve the use of a structured self-administered questionnaires to health workers (Doctors, Nurses, Pharmacist, Laboratory scientist and Radiologist etc) in Sir Yahaya Memorial Hospital, B/kebbi.

The management is wishes you the best in your conducting this research.

Thank you for your usual cooperation please.

Umar Ahmad G/gaji
Hospital Secretary
For:- Perm. Sec./C.M.D

APPENDIX L

University of Witwatersrand Registrar's approval letter.

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

OFFICE OF THE DEPUTY REGISTRAR

07 June 2019

Mustapha Aliero Halidu
Student number 1966648
MA Medicine (Dissertation)
School of Therapeutics

TO WHOM IT MAY CONCERN

"Knowledge, attitudes and perceptions on the management of malaria and evaluation of an efficacy of commercially available mosquito repellents in Johannesburg, South Africa"

This letter serves to confirm that the above project has received permission to be conducted on University premises, and/or involving staff and/or students of the University as research participants. In undertaking this research, you agree to abide by all University regulations for conducting research on campus and to respect participants' rights to withdraw from participation at any time.

If you are conducting research on certain student cohorts, year groups or courses within specific Schools and within the teaching term, permission must be sought from Heads of School or individual academics.

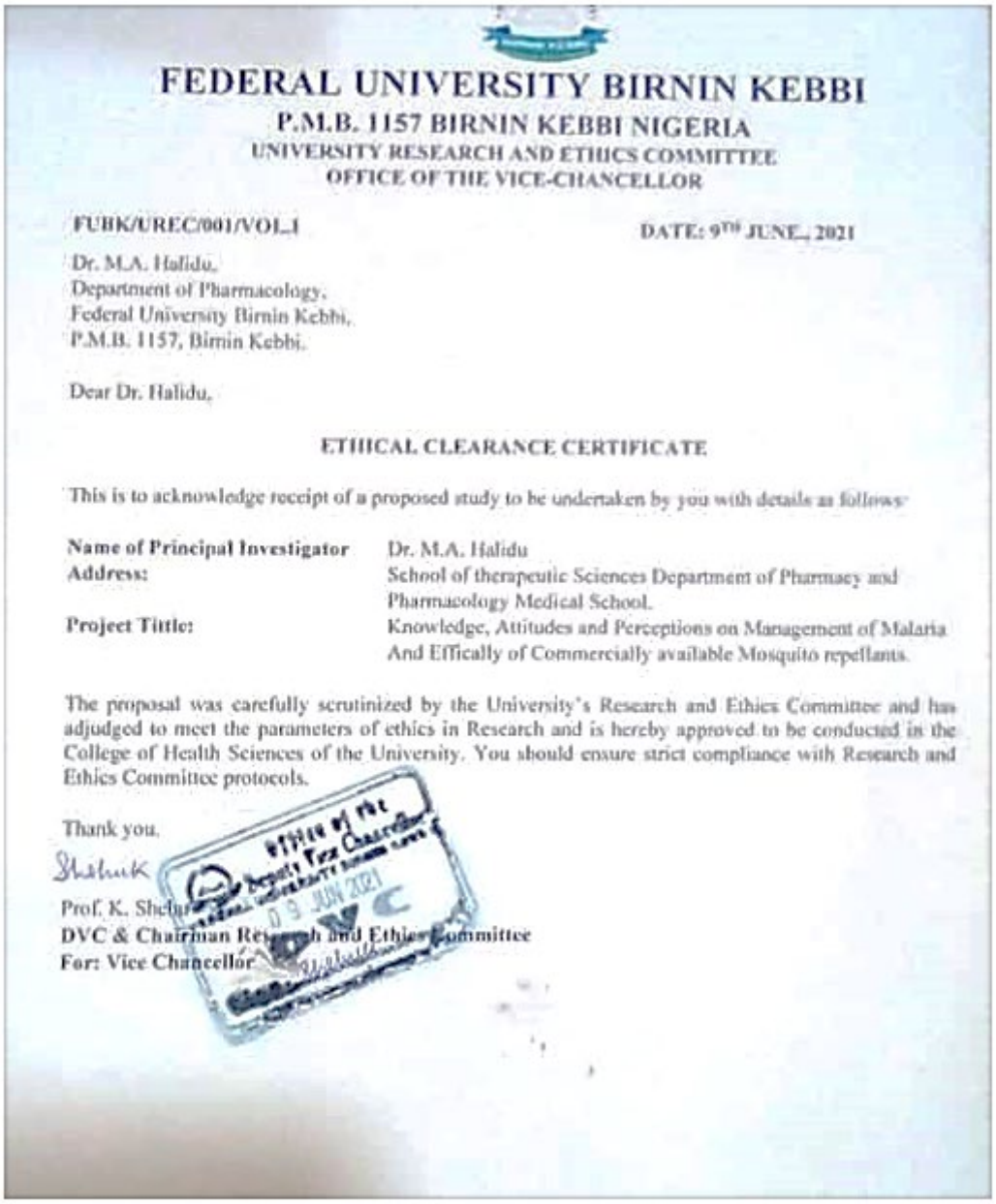
No research can commence before ethical clearance has been obtained. Kindly forward a copy of the clearance certificate to this office.

Carol Crosley
University Registrar

Private Bag 3, Wits, 2050, South Africa | T +27 11 717 1204/8 | F +27 86 553 2271 | www.wits.ac.za

APPENDIX M

Federal University Birnin Kebbi Registrar's approval letter. Ggp



FEDERAL UNIVERSITY BIRNIN KEBBI
P.M.B. 1157 BIRNIN KEBBI NIGERIA
UNIVERSITY RESEARCH AND ETHICS COMMITTEE
OFFICE OF THE VICE-CHANCELLOR

FUBK/UREC/001/VOL.1 DATE: 9TH JUNE., 2021

Dr. M.A. Halidu,
Department of Pharmacology,
Federal University Birnin Kebbi,
P.M.B. 1157, Birnin Kebbi.

Dear Dr. Halidu,

ETHICAL CLEARANCE CERTIFICATE

This is to acknowledge receipt of a proposed study to be undertaken by you with details as follows:

Name of Principal Investigator	Dr. M.A. Halidu
Address:	School of therapeutic Sciences Department of Pharmacy and Pharmacology Medical School.
Project Tittle:	Knowledge, Attitudes and Perceptions on Management of Malaria And Effically of Commercially available Mosquito repellants.

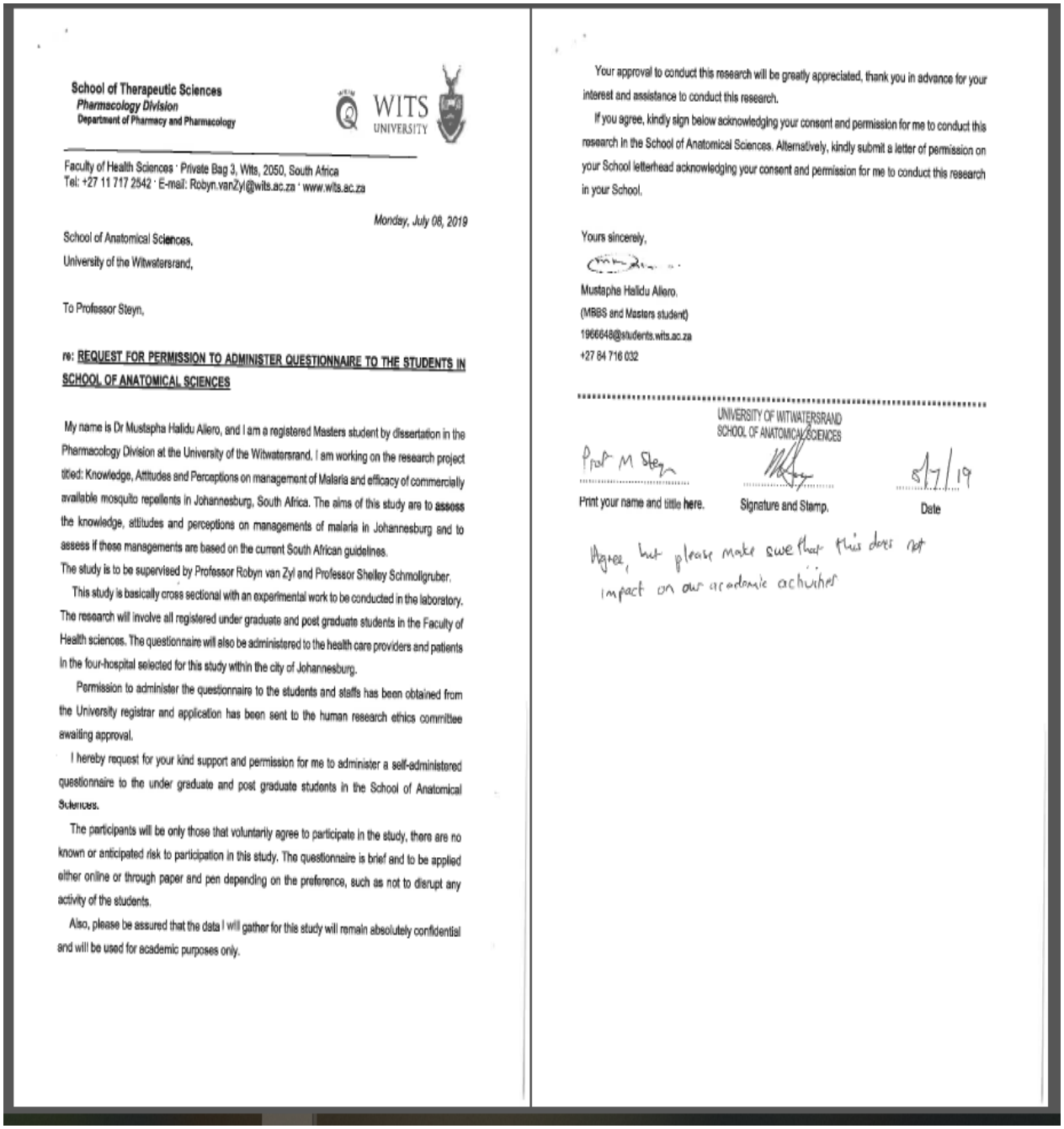
The proposal was carefully scrutinized by the University's Research and Ethics Committee and has adjudged to meet the parameters of ethics in Research and is hereby approved to be conducted in the College of Health Sciences of the University. You should ensure strict compliance with Research and Ethics Committee protocols.

Thank you.

Prof. K. Shehu
DVC & Chairman Research and Ethics Committee
For: Vice Chancellor

APPENDIX N

Head of school of anatomical sciences approval letter.



School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

Faculty of Health Sciences · Private Bag 3, Wits, 2050, South Africa
Tel: +27 11 717 2542 · E-mail: Robyn.vanZyl@wits.ac.za · www.wits.ac.za

Monday, July 08, 2019

School of Anatomical Sciences,
University of the Witwatersrand,

To Professor Steyn,

re: **REQUEST FOR PERMISSION TO ADMINISTER QUESTIONNAIRE TO THE STUDENTS IN SCHOOL OF ANATOMICAL SCIENCES**

My name is Dr Mustapha Halidu Allero, and I am a registered Masters student by dissertation in the Pharmacology Division at the University of the Witwatersrand. I am working on the research project titled: Knowledge, Attitudes and Perceptions on management of Malaria and efficacy of commercially available mosquito repellents in Johannesburg, South Africa. The aims of this study are to assess the knowledge, attitudes and perceptions on managements of malaria in Johannesburg and to assess if these managements are based on the current South African guidelines.
The study is to be supervised by Professor Robyn van Zyl and Professor Shelley Schmollgruber.

This study is basically cross sectional with an experimental work to be conducted in the laboratory. The research will involve all registered under graduate and post graduate students in the Faculty of Health sciences. The questionnaire will also be administered to the health care providers and patients in the four-hospital selected for this study within the city of Johannesburg.

Permission to administer the questionnaire to the students and staffs has been obtained from the University registrar and application has been sent to the human research ethics committee awaiting approval.

I hereby request for your kind support and permission for me to administer a self-administered questionnaire to the under graduate and post graduate students in the School of Anatomical Sciences.

The participants will be only those that voluntarily agree to participate in the study, there are no known or anticipated risk to participation in this study. The questionnaire is brief and to be applied either online or through paper and pen depending on the preference, such as not to disrupt any activity of the students.

Also, please be assured that the data I will gather for this study will remain absolutely confidential and will be used for academic purposes only.

Your approval to conduct this research will be greatly appreciated, thank you in advance for your interest and assistance to conduct this research.

If you agree, kindly sign below acknowledging your consent and permission for me to conduct this research in the School of Anatomical Sciences. Alternatively, kindly submit a letter of permission on your School letterhead acknowledging your consent and permission for me to conduct this research in your School.

Yours sincerely,

Mustapha Halidu Allero,
(MBBS and Masters student)
1966648@students.wits.ac.za
+27 84 716 032

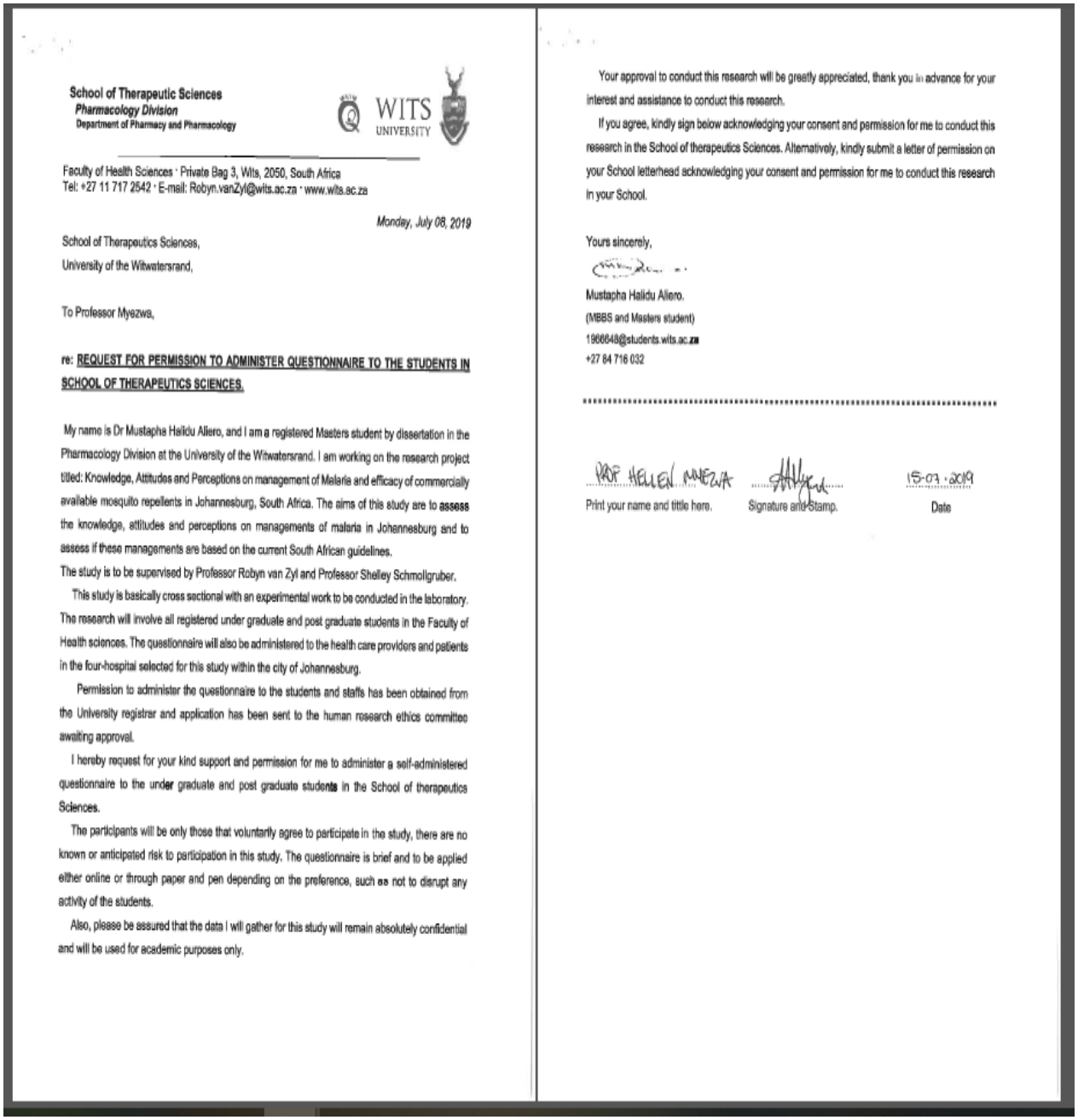
UNIVERSITY OF WITWATERSRAND
SCHOOL OF ANATOMICAL SCIENCES

Prof M Steyn — Print your name and title here.
Signature and Stamp.
8/7/19 — Date

Agree, but please make sure that this does not impact on our academic activities

APPENDIX O

Head of School of Therapeutic Sciences approval letter.



School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

Faculty of Health Sciences · Private Bag 3, Wits, 2050, South Africa
Tel: +27 11 717 2542 · E-mail: Robyn.vanZyl@wits.ac.za · www.wits.ac.za

Monday, July 08, 2019

School of Therapeutics Sciences,
University of the Witwatersrand,

To Professor Myezwa,

re: **REQUEST FOR PERMISSION TO ADMINISTER QUESTIONNAIRE TO THE STUDENTS IN SCHOOL OF THERAPEUTICS SCIENCES.**

My name is Dr Mustapha Halidu Allero, and I am a registered Masters student by dissertation in the Pharmacology Division at the University of the Witwatersrand. I am working on the research project titled: Knowledge, Attitudes and Perceptions on management of Malaria and efficacy of commercially available mosquito repellents in Johannesburg, South Africa. The aims of this study are to assess the knowledge, attitudes and perceptions on managements of malaria in Johannesburg and to assess if these managements are based on the current South African guidelines.

The study is to be supervised by Professor Robyn van Zyl and Professor Shelley Schmollgruber.

This study is basically cross sectional with an experimental work to be conducted in the laboratory. The research will involve all registered under graduate and post graduate students in the Faculty of Health sciences. The questionnaire will also be administered to the health care providers and patients in the four-hospital selected for this study within the city of Johannesburg.

Permission to administer the questionnaire to the students and staffs has been obtained from the University registrar and application has been sent to the human research ethics committee awaiting approval.

I hereby request for your kind support and permission for me to administer a self-administered questionnaire to the under graduate and post graduate students in the School of therapeutics Sciences.

The participants will be only those that voluntarily agree to participate in the study, there are no known or anticipated risk to participation in this study. The questionnaire is brief and to be applied either online or through paper and pen depending on the preference, such as not to disrupt any activity of the students.

Also, please be assured that the data I will gather for this study will remain absolutely confidential and will be used for academic purposes only.

Your approval to conduct this research will be greatly appreciated, thank you in advance for your interest and assistance to conduct this research.

If you agree, kindly sign below acknowledging your consent and permission for me to conduct this research in the School of therapeutics Sciences. Alternatively, kindly submit a letter of permission on your School letterhead acknowledging your consent and permission for me to conduct this research in your School.

Yours sincerely,

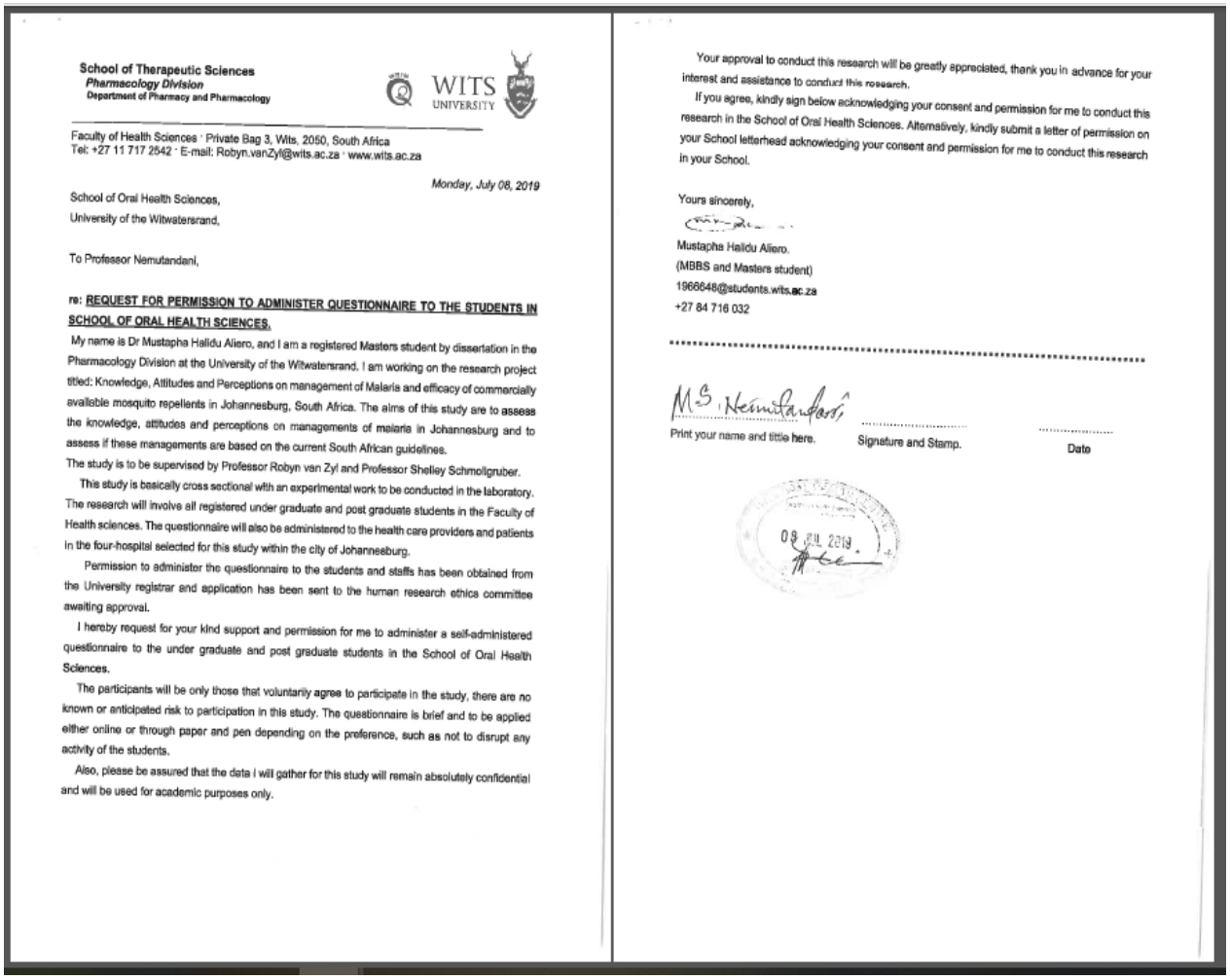
Mustapha Halidu Allero.
(MBBS and Masters student)
1966648@students.wits.ac.za
+27 84 716 032

PROF HELLEN MNEZWA — Signature and Stamp. — 15-07-2019

Print your name and tittle here. — Date

APPENDIX P

Head of school of oral health sciences approval letter.



School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

Faculty of Health Sciences · Private Bag 3, Wits, 2050, South Africa
Tel: +27 11 717 2542 · E-mail: Robyn.vanZyl@wits.ac.za · www.wits.ac.za

Monday, July 08, 2019

School of Oral Health Sciences,
University of the Witwatersrand,

To Professor Nemutandani,

re: **REQUEST FOR PERMISSION TO ADMINISTER QUESTIONNAIRE TO THE STUDENTS IN SCHOOL OF ORAL HEALTH SCIENCES.**

My name is Dr Mustapha Halidu Aliero, and I am a registered Masters student by dissertation in the Pharmacology Division at the University of the Witwatersrand. I am working on the research project titled: Knowledge, Attitudes and Perceptions on management of Malaria and efficacy of commercially available mosquito repellents in Johannesburg, South Africa. The aims of this study are to assess the knowledge, attitudes and perceptions on managements of malaria in Johannesburg and to assess if these managements are based on the current South African guidelines.
The study is to be supervised by Professor Robyn van Zyl and Professor Shelley Schmollgruber.

This study is basically cross sectional with an experimental work to be conducted in the laboratory. The research will involve all registered under graduate and post graduate students in the Faculty of Health sciences. The questionnaire will also be administered to the health care providers and patients in the four-hospital selected for this study within the city of Johannesburg.

Permission to administer the questionnaire to the students and staffs has been obtained from the University registrar and application has been sent to the human research ethics committee awaiting approval.

I hereby request for your kind support and permission for me to administer a self-administered questionnaire to the under graduate and post graduate students in the School of Oral Health Sciences.

The participants will be only those that voluntarily agree to participate in the study, there are no known or anticipated risk to participation in this study. The questionnaire is brief and to be applied either online or through paper and pen depending on the preference, such as not to disrupt any activity of the students.

Also, please be assured that the data I will gather for this study will remain absolutely confidential and will be used for academic purposes only.

Your approval to conduct this research will be greatly appreciated, thank you in advance for your interest and assistance to conduct this research.

If you agree, kindly sign below acknowledging your consent and permission for me to conduct this research in the School of Oral Health Sciences. Alternatively, kindly submit a letter of permission on your School letterhead acknowledging your consent and permission for me to conduct this research in your School.

Yours sincerely,

Mustapha Halidu Aliero.
(MBBS and Masters student)
1966648@students.wits.ac.za
+27 84 716 032

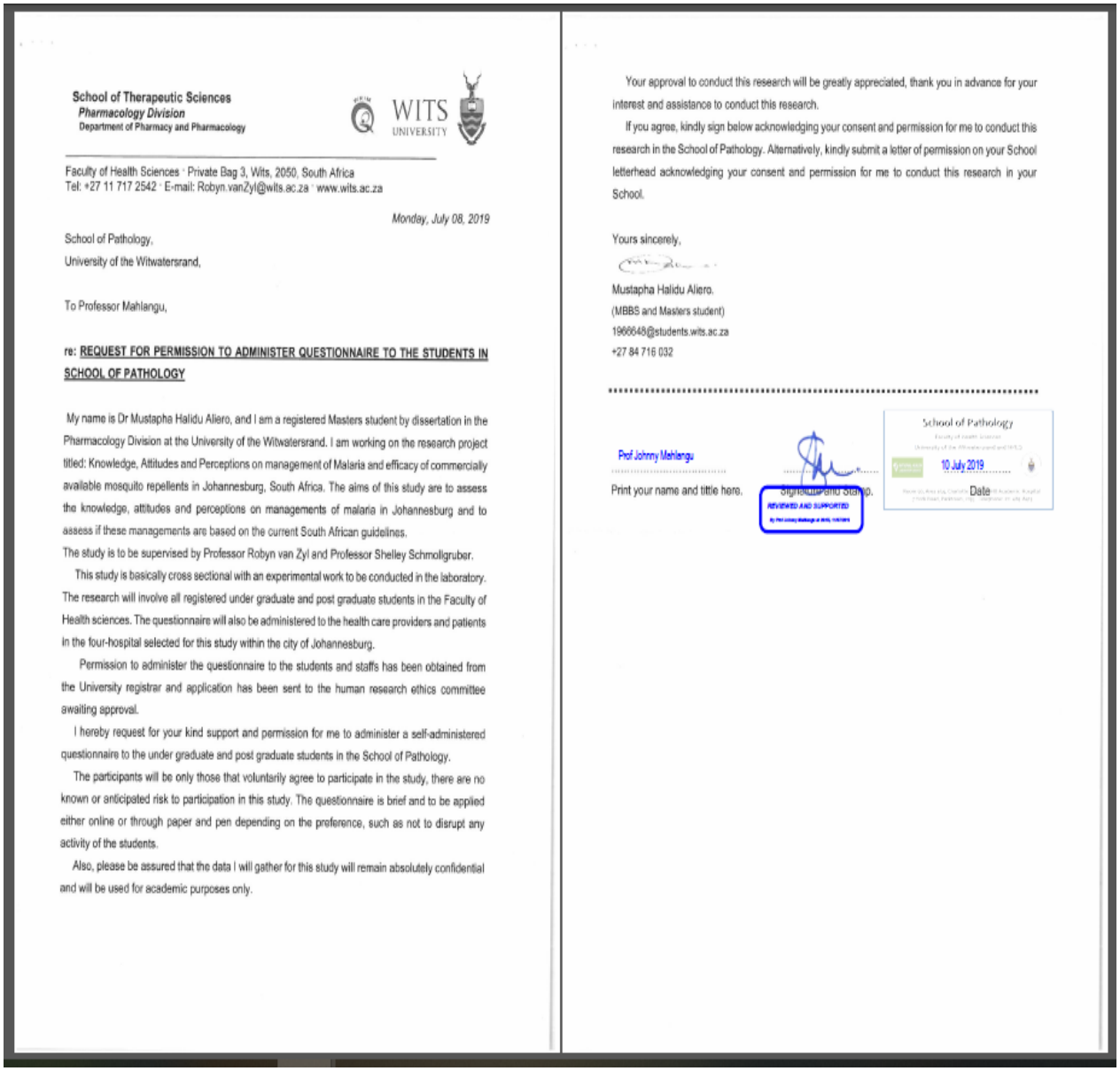
M.S. Nemutandani

Print your name and title here. Signature and Stamp. Date

08 JUL 2019

APPENDIX Q

Head of School of Pathology approval letter.



School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

Faculty of Health Sciences · Private Bag 3, Wits, 2050, South Africa
Tel: +27 11 717 2542 · E-mail: Robyn.vanZyl@wits.ac.za · www.wits.ac.za

Monday, July 08, 2019

School of Pathology,
University of the Witwatersrand,

To Professor Mahlangu,

re: **REQUEST FOR PERMISSION TO ADMINISTER QUESTIONNAIRE TO THE STUDENTS IN SCHOOL OF PATHOLOGY**

My name is Dr Mustapha Halidu Aliero, and I am a registered Masters student by dissertation in the Pharmacology Division at the University of the Witwatersrand. I am working on the research project titled: Knowledge, Attitudes and Perceptions on management of Malaria and efficacy of commercially available mosquito repellents in Johannesburg, South Africa. The aims of this study are to assess the knowledge, attitudes and perceptions on managements of malaria in Johannesburg and to assess if these managements are based on the current South African guidelines.
The study is to be supervised by Professor Robyn van Zyl and Professor Shelley Schmollgruber.

This study is basically cross sectional with an experimental work to be conducted in the laboratory. The research will involve all registered under graduate and post graduate students in the Faculty of Health sciences. The questionnaire will also be administered to the health care providers and patients in the four-hospital selected for this study within the city of Johannesburg.

Permission to administer the questionnaire to the students and staffs has been obtained from the University registrar and application has been sent to the human research ethics committee awaiting approval.

I hereby request for your kind support and permission for me to administer a self-administered questionnaire to the under graduate and post graduate students in the School of Pathology.

The participants will be only those that voluntarily agree to participate in the study, there are no known or anticipated risk to participation in this study. The questionnaire is brief and to be applied either online or through paper and pen depending on the preference, such as not to disrupt any activity of the students.

Also, please be assured that the data I will gather for this study will remain absolutely confidential and will be used for academic purposes only.

Your approval to conduct this research will be greatly appreciated, thank you in advance for your interest and assistance to conduct this research.

If you agree, kindly sign below acknowledging your consent and permission for me to conduct this research in the School of Pathology. Alternatively, kindly submit a letter of permission on your School letterhead acknowledging your consent and permission for me to conduct this research in your School.

Yours sincerely,

Mustapha Halidu Aliero.
(MBBS and Masters student)
1966648@students.wits.ac.za
+27 84 716 032

Prof Johnny Mahlangu
Print your name and tittle here.

Signature and Stamp.

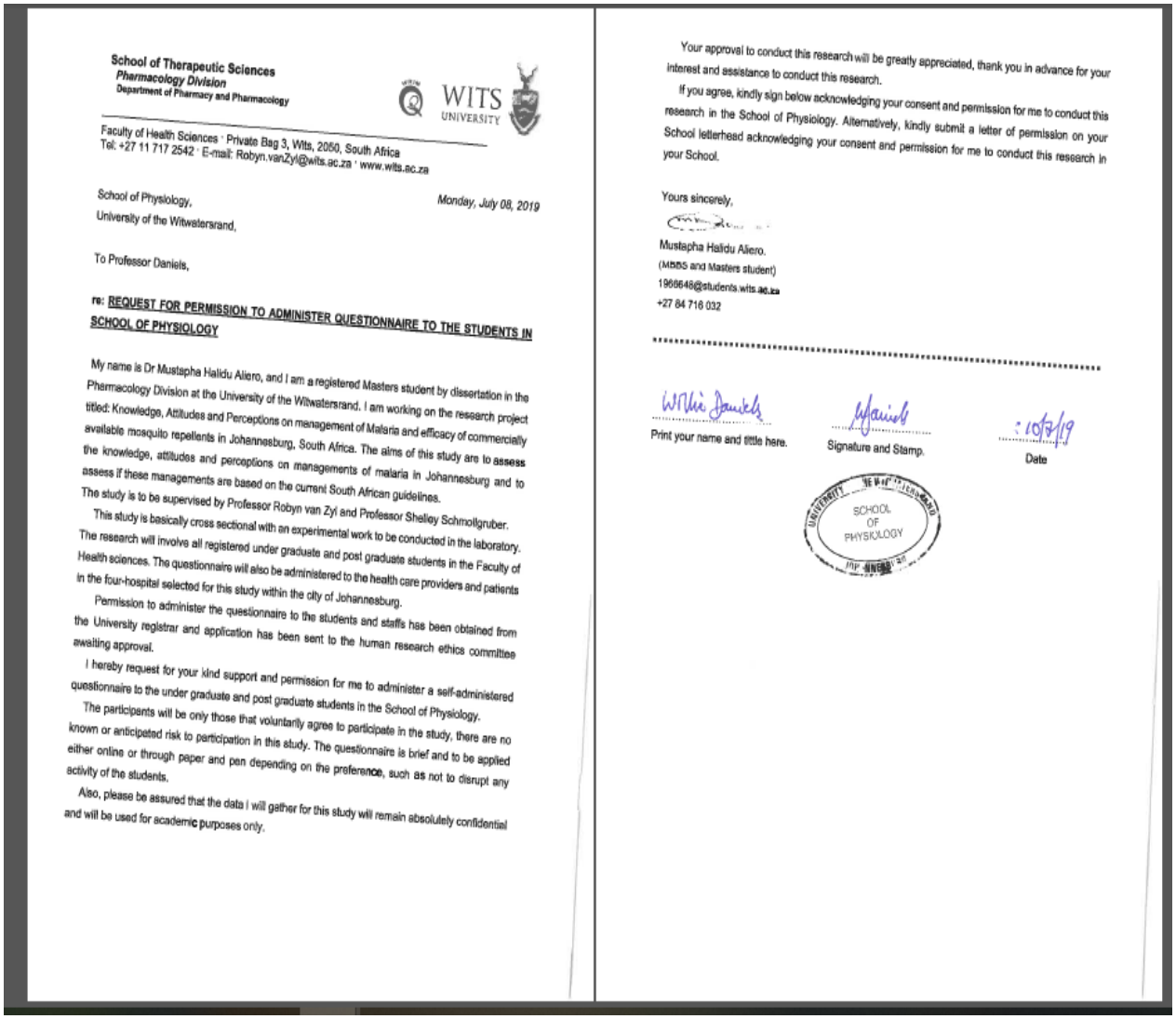
REVIEWED AND SUPPORTED

School of Pathology

10 July 2019
Date

APPENDIX R

Head of school physiology approval letter.



School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

Faculty of Health Sciences · Private Bag 3, Wits, 2050, South Africa
Tel: +27 11 717 2542 · E-mail: Robyn.vanZyl@wits.ac.za · www.wits.ac.za

School of Physiology,
University of the Witwatersrand,

Monday, July 08, 2019

To Professor Daniels,

re: **REQUEST FOR PERMISSION TO ADMINISTER QUESTIONNAIRE TO THE STUDENTS IN SCHOOL OF PHYSIOLOGY**

My name is Dr Mustapha Halidu Allero, and I am a registered Masters student by dissertation in the Pharmacology Division at the University of the Witwatersrand. I am working on the research project titled: Knowledge, Attitudes and Perceptions on management of Malaria and efficacy of commercially available mosquito repellents in Johannesburg, South Africa. The aims of this study are to assess the knowledge, attitudes and perceptions on managements of malaria in Johannesburg and to assess if these managements are based on the current South African guidelines.
The study is to be supervised by Professor Robyn van Zyl and Professor Shelley Schmollgruber.

This study is basically cross sectional with an experimental work to be conducted in the laboratory. The research will involve all registered under graduate and post graduate students in the Faculty of Health sciences. The questionnaire will also be administered to the health care providers and patients in the four-hospital selected for this study within the city of Johannesburg.

Permission to administer the questionnaire to the students and staffs has been obtained from the University registrar and application has been sent to the human research ethics committee awaiting approval.

I hereby request for your kind support and permission for me to administer a self-administered questionnaire to the under graduate and post graduate students in the School of Physiology.

The participants will be only those that voluntarily agree to participate in the study, there are no known or anticipated risk to participation in this study. The questionnaire is brief and to be applied either online or through paper and pen depending on the preference, such as not to disrupt any activity of the students.

Also, please be assured that the data I will gather for this study will remain absolutely confidential and will be used for academic purposes only.

Your approval to conduct this research will be greatly appreciated, thank you in advance for your interest and assistance to conduct this research.

If you agree, kindly sign below acknowledging your consent and permission for me to conduct this research in the School of Physiology. Alternatively, kindly submit a letter of permission on your School letterhead acknowledging your consent and permission for me to conduct this research in your School.

Yours sincerely,

Mustapha Halidu Allero.
(MBBS and Masters student)
1966648@students.wits.ac.za
+27 84 716 032

Print your name and title here.

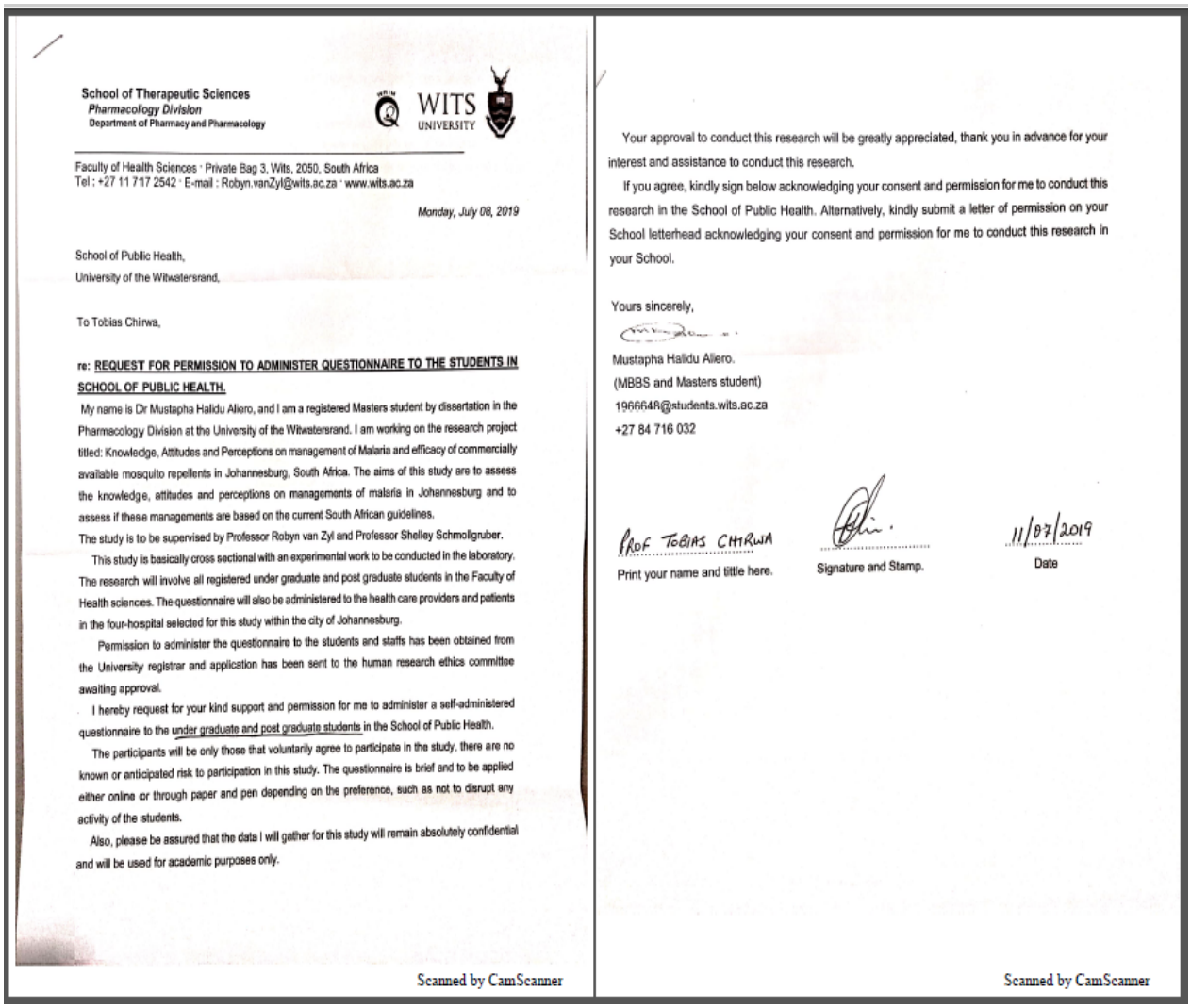
Signature and Stamp.

Date: 10/7/19

SCHOOL OF PHYSIOLOGY

APPENDIX S

Head of School Public Health approval letter.



School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

Faculty of Health Sciences · Private Bag 3, Wits, 2050, South Africa
Tel : +27 11 717 2542 · E-mail : Robyn.vanZyl@wits.ac.za · www.wits.ac.za

Monday, July 08, 2019

School of Public Health,
University of the Witwatersrand.

To Tobias Chirwa,

re: **REQUEST FOR PERMISSION TO ADMINISTER QUESTIONNAIRE TO THE STUDENTS IN SCHOOL OF PUBLIC HEALTH.**

My name is Dr Mustapha Halidu Aliero, and I am a registered Masters student by dissertation in the Pharmacology Division at the University of the Witwatersrand. I am working on the research project titled: Knowledge, Attitudes and Perceptions on management of Malaria and efficacy of commercially available mosquito repellents in Johannesburg, South Africa. The aims of this study are to assess the knowledge, attitudes and perceptions on managements of malaria in Johannesburg and to assess if these managements are based on the current South African guidelines.

The study is to be supervised by Professor Robyn van Zyl and Professor Shelley Schmollgruber.

This study is basically cross sectional with an experimental work to be conducted in the laboratory. The research will involve all registered under graduate and post graduate students in the Faculty of Health sciences. The questionnaire will also be administered to the health care providers and patients in the four-hospital selected for this study within the city of Johannesburg.

Permission to administer the questionnaire to the students and staffs has been obtained from the University registrar and application has been sent to the human research ethics committee awaiting approval.

I hereby request for your kind support and permission for me to administer a self-administered questionnaire to the under graduate and post graduate students in the School of Public Health.

The participants will be only those that voluntarily agree to participate in the study, there are no known or anticipated risk to participation in this study. The questionnaire is brief and to be applied either online or through paper and pen depending on the preference, such as not to disrupt any activity of the students.

Also, please be assured that the data I will gather for this study will remain absolutely confidential and will be used for academic purposes only.

Scanned by CamScanner

Your approval to conduct this research will be greatly appreciated, thank you in advance for your interest and assistance to conduct this research.

If you agree, kindly sign below acknowledging your consent and permission for me to conduct this research in the School of Public Health. Alternatively, kindly submit a letter of permission on your School letterhead acknowledging your consent and permission for me to conduct this research in your School.

Yours sincerely,

Mustapha Halidu Aliero.
(MBBS and Masters student)
196664R@students.wits.ac.za
+27 84 716 032

PROF TOBIAS CHIRWA
Print your name and tittle here.

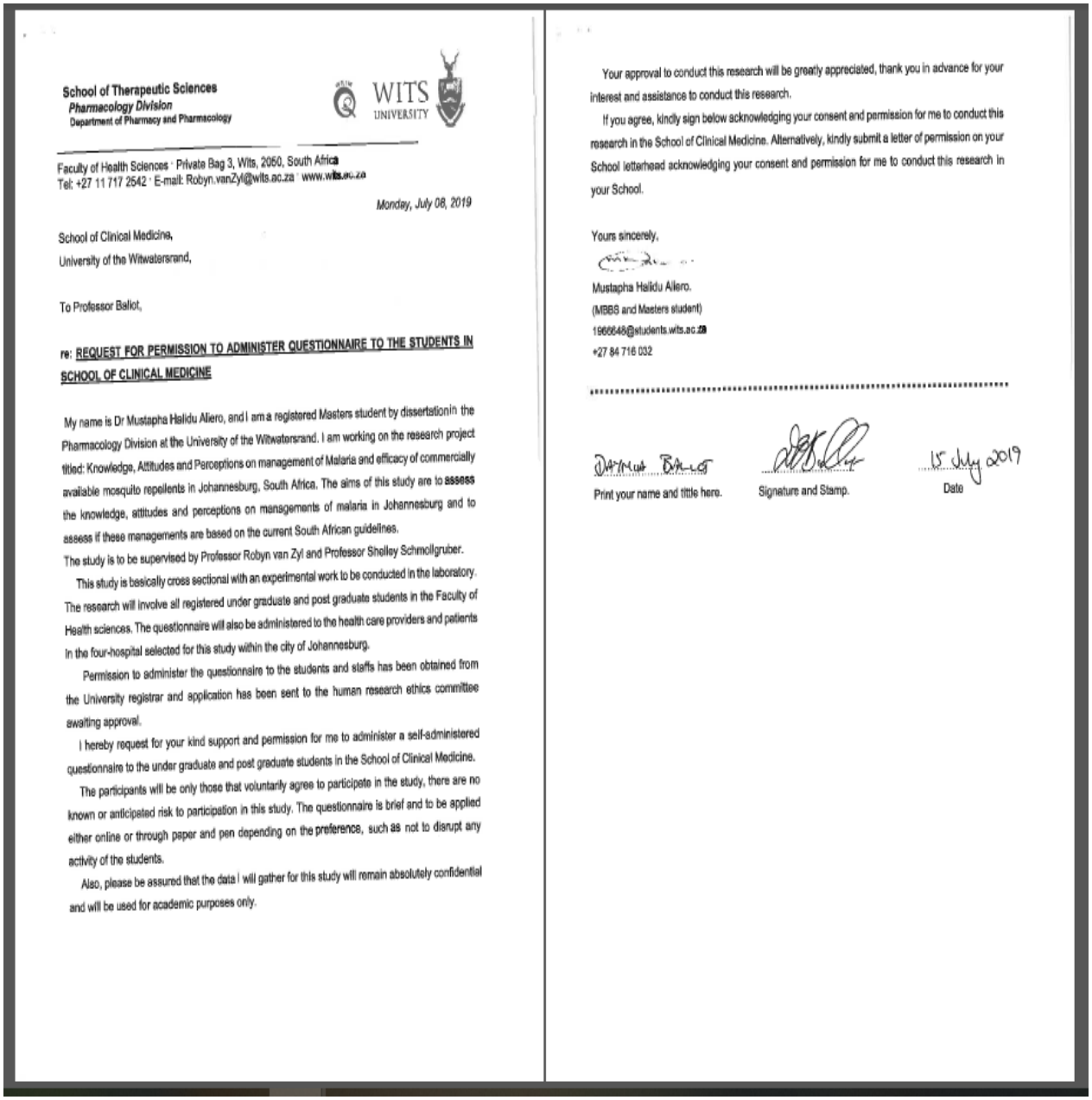
Signature and Stamp.

11/07/2019
Date

Scanned by CamScanner

APPENDIX T

Head of School of Clinical Medicine approval letter.



School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

Faculty of Health Sciences · Private Bag 3, Wits, 2050, South Africa
Tel: +27 11 717 2542 · E-mail: Robyn.vanZyl@wits.ac.za · www.wits.ac.za

Monday, July 08, 2019

School of Clinical Medicine,
University of the Witwatersrand,

To Professor Balliot,

re: **REQUEST FOR PERMISSION TO ADMINISTER QUESTIONNAIRE TO THE STUDENTS IN SCHOOL OF CLINICAL MEDICINE**

My name is Dr Mustapha Halidu Allero, and I am a registered Masters student by dissertationin the Pharmacology Division at the University of the Witwatersrand. I am working on the research project titled: Knowledge, Attitudes and Perceptions on management of Malaria and efficacy of commercially available mosquito repellents in Johannesburg, South Africa. The aims of this study are to assess the knowledge, attitudes and perceptions on managements of malaria in Johannesburg and to assess if these managements are based on the current South African guidelines.
The study is to be supervised by Professor Robyn van Zyl and Professor Shelley Schmollgruber.

This study is basically cross sectional with an experimental work to be conducted in the laboratory. The research will involve all registered under graduate and post graduate students in the Faculty of Health sciences. The questionnaire will also be administered to the health care providers and patients in the four-hospital selected for this study within the city of Johannesburg.

Permission to administer the questionnaire to the students and staffs has been obtained from the University registrar and application has been sent to the human research ethics committee awaiting approval.

I hereby request for your kind support and permission for me to administer a self-administered questionnaire to the under graduate and post graduate students in the School of Clinical Medicine.

The participants will be only those that voluntarily agree to participate in the study, there are no known or anticipated risk to participation in this study. The questionnaire is brief and to be applied either online or through paper and pen depending on the preference, such as not to disrupt any activity of the students.

Also, please be assured that the data I will gather for this study will remain absolutely confidential and will be used for academic purposes only.

Your approval to conduct this research will be greatly appreciated, thank you in advance for your interest and assistance to conduct this research.

If you agree, kindly sign below acknowledging your consent and permission for me to conduct this research in the School of Clinical Medicine. Alternatively, kindly submit a letter of permission on your School letterhead acknowledging your consent and permission for me to conduct this research in your School.

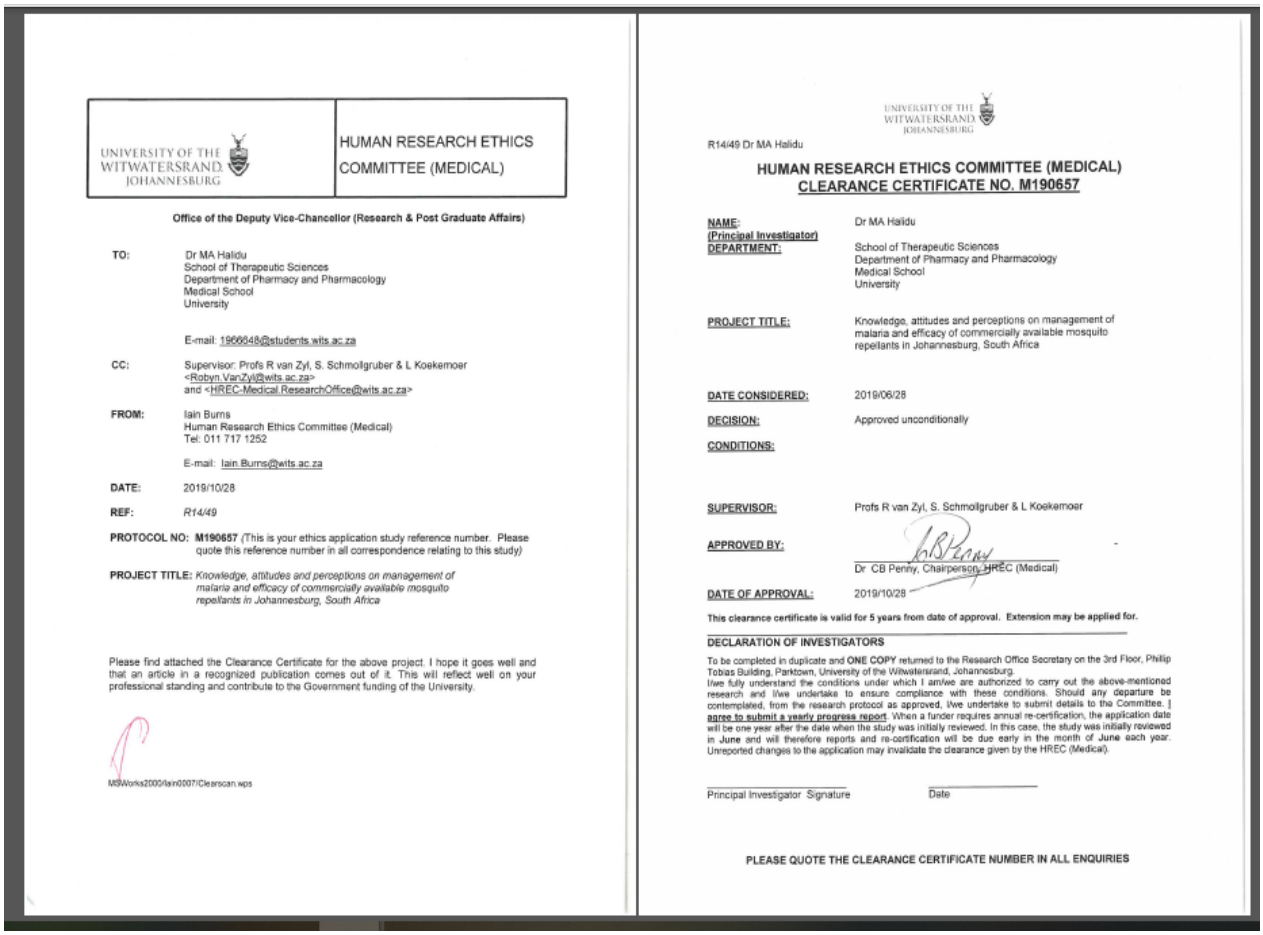
Yours sincerely,

Mustapha Halidu Allero.
(MBBS and Masters student)
1966648@students.wits.ac.za
+27 84 716 032

Print your name and title here. Signature and Stamp. 15 July 2019 Date

APPENDIX U

University of Witwatersrand Human ethics research committee approval certificate Part One and Part two).



UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Dr MA Halidu
School of Therapeutic Sciences
Department of Pharmacy and Pharmacology
Medical School
University

E-mail: 1966648@students.wits.ac.za

CC: Supervisor: Profs R van Zyl, S. Schmoilgruber & L Koekemoer
<Robyn.VanZyl@wits.ac.za>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 2019/10/28

REF: *R14/49*

PROTOCOL NO: **M190657** *(This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)*

PROJECT TITLE: *Knowledge, attitudes and perceptions on management of malaria and efficacy of commercially available mosquito repellants in Johannesburg, South Africa*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr MA Halidu

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M190657

NAME: Dr MA Halidu
(Principal Investigator)
DEPARTMENT: School of Therapeutic Sciences
Department of Pharmacy and Pharmacology
Medical School
University

PROJECT TITLE: Knowledge, attitudes and perceptions on management of malaria and efficacy of commercially available mosquito repellants in Johannesburg, South Africa

DATE CONSIDERED: 2019/06/28

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Profs R van Zyl, S. Schmoilgruber & L Koekemoer

APPROVED BY:
Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 2019/10/28

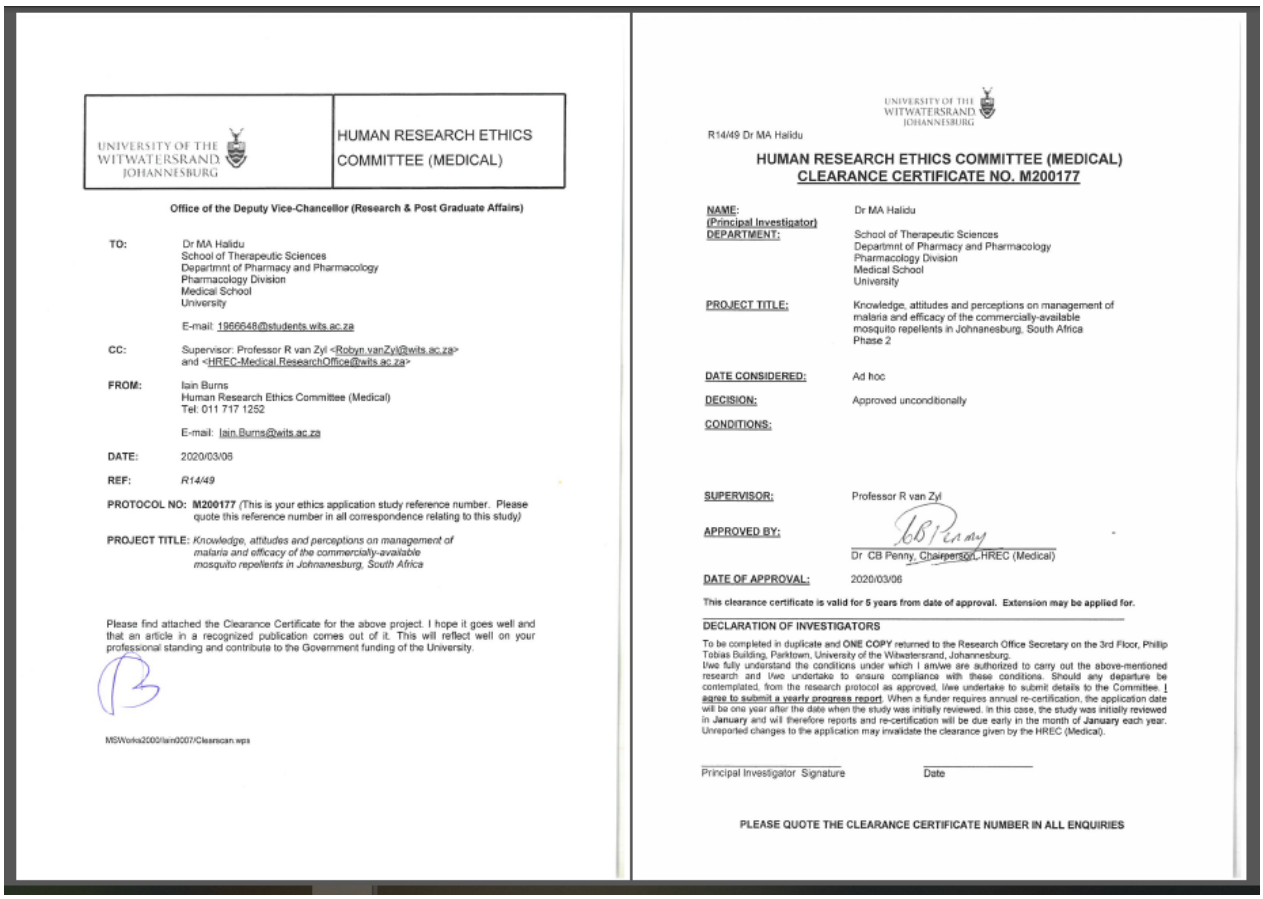
This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report.** When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in June and will therefore reports and re-certification will be due early in the month of June each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES



UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Dr MA Halidu
School of Therapeutic Sciences
Departmnt of Pharmacy and Pharmacology
Pharmacology Division
Medical School
University

E-mail: 1966648@students.wits.ac.za

CC: Supervisor: Professor R van Zyl <Robyn.vanZyl@wits.ac.za>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 2020/03/06

REF: *R14/49*

PROTOCOL NO: **M200177** *(This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)*

PROJECT TITLE: *Knowledge, attitudes and perceptions on management of malaria and efficacy of the commercially-available mosquito repellents in Johnanesburg, South Africa*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr MA Halidu

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M200177

NAME: (Principal Investigator)	Dr MA Halidu
DEPARTMENT:	School of Therapeutic Sciences Departmnt of Pharmacy and Pharmacology Pharmacology Division Medical School University
PROJECT TITLE:	Knowledge, attitudes and perceptions on management of malaria and efficacy of the commercially-available mosquito repellents in Johnanesburg, South Africa Phase 2
DATE CONSIDERED:	Ad hoc
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Professor R van Zyl
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2020/03/06

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

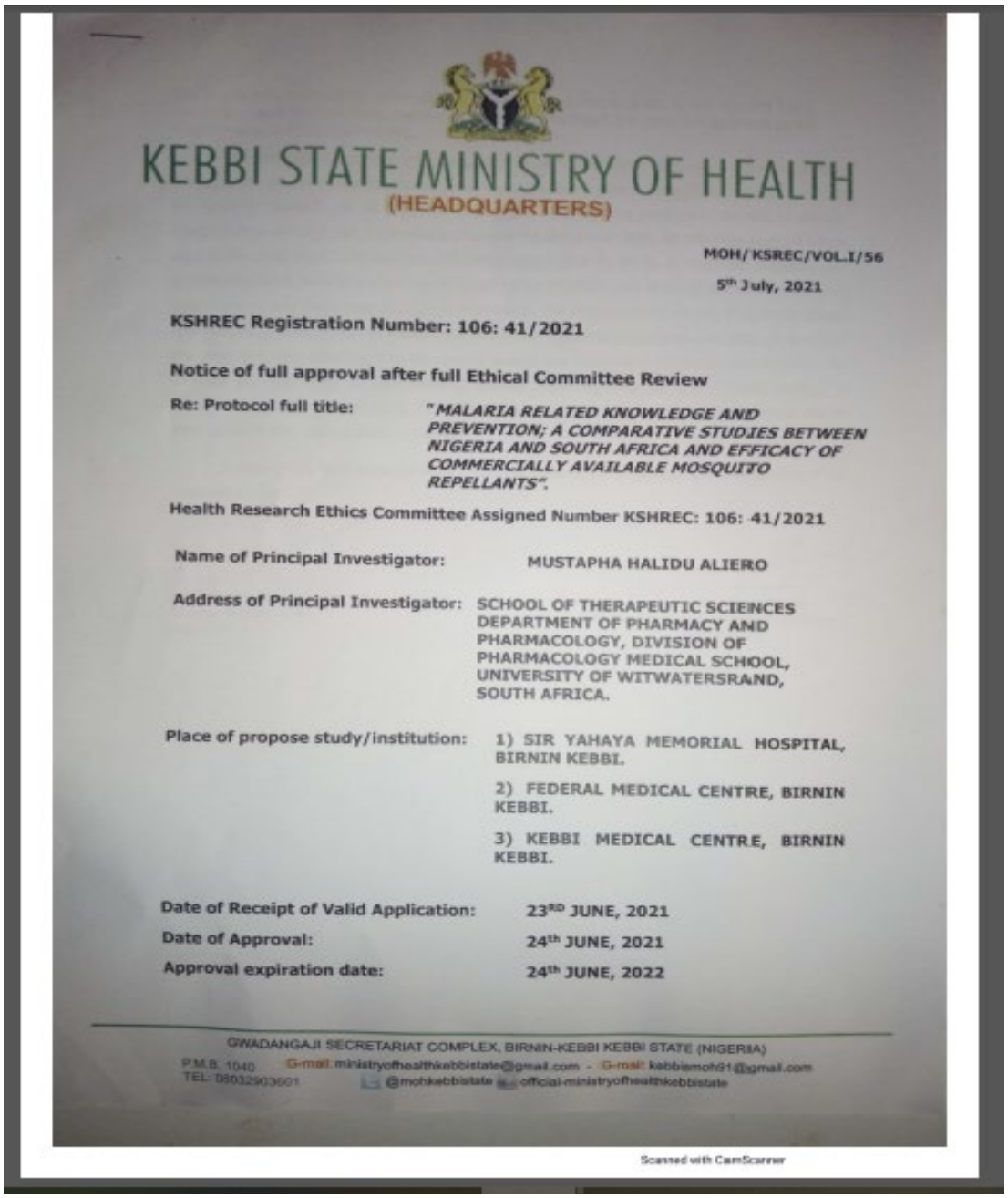
To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report.** When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **January** and will therefore reports and re-certification will be due early in the month of **January** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

APPENDIX V

Federal University Birnin Kebbi and Kebbi State Ministry of Health Ethics Approval Letters.



KEBBI STATE MINISTRY OF HEALTH
(HEADQUARTERS)

MOH/KSREC/VOL.I/56

5th July, 2021

KSHREC Registration Number: 106: 41/2021

Notice of full approval after full Ethical Committee Review

Re: Protocol full title: *"MALARIA RELATED KNOWLEDGE AND PREVENTION; A COMPARATIVE STUDIES BETWEEN NIGERIA AND SOUTH AFRICA AND EFFICACY OF COMMERCIALLY AVAILABLE MOSQUITO REPELLANTS".*

Health Research Ethics Committee Assigned Number KSHREC: 106: 41/2021

Name of Principal Investigator: MUSTAPHA HALIDU ALIERO

Address of Principal Investigator: SCHOOL OF THERAPEUTIC SCIENCES DEPARTMENT OF PHARMACY AND PHARMACOLOGY, DIVISION OF PHARMACOLOGY MEDICAL SCHOOL, UNIVERSITY OF WITWATERSRAND, SOUTH AFRICA.

Place of propose study/institution:
1) SIR YAHAYA MEMORIAL HOSPITAL, BIRNIN KEBBI.
2) FEDERAL MEDICAL CENTRE, BIRNIN KEBBI.
3) KEBBI MEDICAL CENTRE, BIRNIN KEBBI.

Date of Receipt of Valid Application: 23RD JUNE, 2021
Date of Approval: 24th JUNE, 2021
Approval expiration date: 24th JUNE, 2022

GWADANGAJI SECRETARIAT COMPLEX, BIRNIN-KEBBI KEBBI STATE (NIGERIA)
P.M.B. 1040 G-mail: ministryofhealthkebbistate@gmail.com - G-mail: kebbismoh91@gmail.com
TEL: 08032903601 @mohkebbistate official-ministryofhealthkebbistate

Scanned with CamScanner

APPENDIX W

Approval of change of title (HREC and FHS post graduate office).

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R49 Dr MA Halidu

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M190657

NAME: (Principal Investigator)	Dr MA Halidu
DEPARTMENT:	School of Therapeutic Sciences Department of Pharmacy and Pharmacology Medical School University
PROJECT TITLE:	*Malaria-related knowledge and prevention practices: a comparative study between South Africa and Nigeria; and efficacy of commercially-available mosquito repellants* ***Change of study title noted on 2021/08/10***
DATE CONSIDERED:	2019/06/28
DECISION:	Approved unconditionally
CONDITIONS:	
NOTE:	If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>
SUPERVISOR:	Profs R van Zyl, S. Schmolgruber & L Koekemoer
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2019/10/28

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report.** When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **June** and therefore reports and re-certification will be due in the month of **June** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator Date

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

28 July 2021
Person No: 1966648
TAA

Dr MA Halidu
Federal University
Kebbi
1157
Nigeria

Dear Dr Mustapha Halidu

Master of Science in Medicine: Change of title of research

I am pleased to inform you that the following change in the title of your Dissertation for the degree of **Master of Science in Medicine** has been approved:

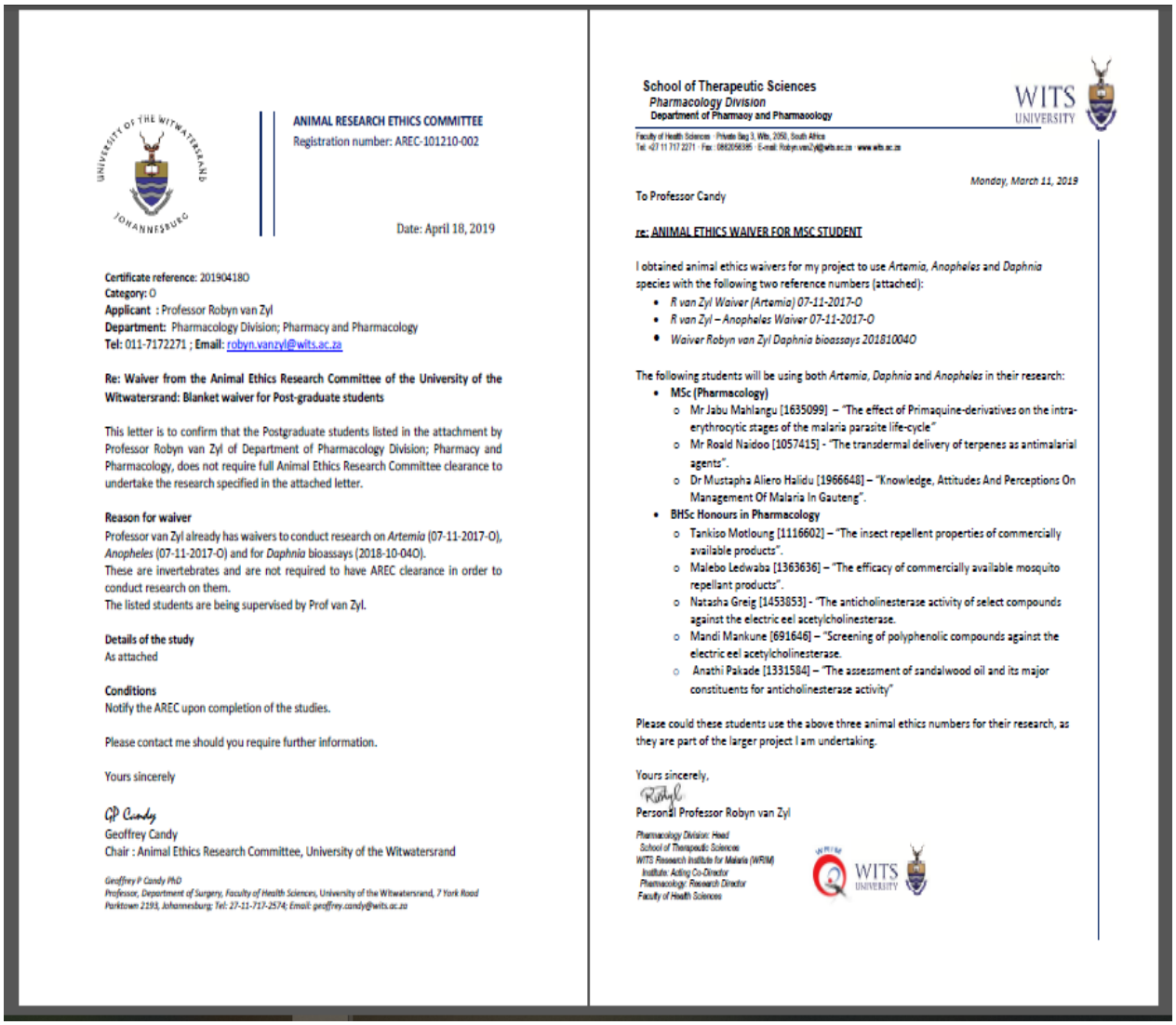
From:	**Knowledge, attitudes and perceptions on the management of Malaria and efficacy of the commercially available mosquitoes repellents in Johannesburg, South Africa**
To:	**Malaria related knowledge and prevention practices: A comparative study between South Africa and Nigeria; and efficacy of commercially available mosquito repellents.**

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

APPENDIX X

Animal Research Ethics Committee *Anopheles* Waiver Certificates for Efficacy Assays.



ANIMAL RESEARCH ETHICS COMMITTEE
Registration number: AREC-101210-002

Date: April 18, 2019

Certificate reference: 20190418O
Category: O
Applicant : Professor Robyn van Zyl
Department: Pharmacology Division; Pharmacy and Pharmacology
Tel: 011-7172271 ; **Email:** robyn.vanzyl@wits.ac.za

Re: Waiver from the Animal Ethics Research Committee of the University of the Witwatersrand: Blanket waiver for Post-graduate students

This letter is to confirm that the Postgraduate students listed in the attachment by Professor Robyn van Zyl of Department of Pharmacology Division; Pharmacy and Pharmacology, does not require full Animal Ethics Research Committee clearance to undertake the research specified in the attached letter.

Reason for waiver
Professor van Zyl already has waivers to conduct research on *Artemia* (07-11-2017-O), *Anopheles* (07-11-2017-O) and for *Daphnia* bioassays (2018-10-04O).
These are invertebrates and are not required to have AREC clearance in order to conduct research on them.
The listed students are being supervised by Prof van Zyl.

Details of the study
As attached

Conditions
Notify the AREC upon completion of the studies.

Please contact me should you require further information.

Yours sincerely

GP Candy
Geoffrey Candy
Chair : Animal Ethics Research Committee, University of the Witwatersrand

Geoffrey P Candy PhD
Professor, Department of Surgery, Faculty of Health Sciences, University of the Witwatersrand, 7 York Road Parktown 2193, Johannesburg; Tel: 27-11-717-2574; Email: geoffrey.candy@wits.ac.za

School of Therapeutic Sciences
Pharmacology Division
Department of Pharmacy and Pharmacology

WITS UNIVERSITY

Faculty of Health Sciences · Private Bag 3, Wits, 2050, South Africa
Tel: +27 11 717 2271 · Fax: 0862056395 · E-mail: Robyn.vanZyl@wits.ac.za · www.wits.ac.za

Monday, March 11, 2019

To Professor Candy

re: ANIMAL ETHICS WAIVER FOR MSC STUDENT

I obtained animal ethics waivers for my project to use *Artemia*, *Anopheles* and *Daphnia* species with the following two reference numbers (attached):

- *R van Zyl Waiver (Artemia) 07-11-2017-O*
- *R van Zyl – Anopheles Waiver 07-11-2017-O*
- *Waiver Robyn van Zyl Daphnia bioassays 20181004O*

The following students will be using both *Artemia*, *Daphnia* and *Anopheles* in their research:

- **MSc (Pharmacology)**
  - Mr Jabu Mahlangu [1635099] – "The effect of Primaquine-derivatives on the intra-erythrocytic stages of the malaria parasite life-cycle"
  - Mr Roald Naidoo [1057415] - "The transdermal delivery of terpenes as antimalarial agents".
  - Dr Mustapha Aliero Halidu [1966648] – "Knowledge, Attitudes And Perceptions On Management Of Malaria In Gauteng".
- **BHSc Honours in Pharmacology**
  - Tankiso Motloung [1116602] – "The insect repellent properties of commercially available products".
  - Malebo Ledwaba [1363636] – "The efficacy of commercially available mosquito repellant products".
  - Natasha Greig [1453853] - "The anticholinesterase activity of select compounds against the electric eel acetylcholinesterase.
  - Mandi Mankune [691646] – "Screening of polyphenolic compounds against the electric eel acetylcholinesterase.
  - Anathi Pakade [1331584] – "The assessment of sandalwood oil and its major constituents for anticholinesterase activity"

Please could these students use the above three animal ethics numbers for their research, as they are part of the larger project I am undertaking.

Yours sincerely,
Personal Professor Robyn van Zyl

Pharmacology Division: Head
School of Therapeutic Sciences
WITS Research Institute for Malaria (WRIM)
Institute: Acting Co-Director
Pharmacology: Research Director
Faculty of Health Sciences

WITS UNIVERSITY

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

ANIMAL RESEARCH ETHICS COMMITTEE (AREC)

Registration number: AREC0101210-002

Solomon Mahlangu House
10th Floor, Room 10004
Jorissen Street
Braamfontein, Johannesburg

7 November 2017

To whom it may concern,

Re: Waiver from Animal Ethics Screening Committee of the University of the Witwatersrand

This letter serves to confirm that Associate Professor Robyn van Zyl (Department of Pharmacy and Pharmacology, School of Therapeutic Sciences, University of the Witwatersrand) does not require full animal ethics clearance for her studies which use *Anopheles* mosquito species to evaluate known or novel synthetic and natural compounds as potential insecticides against *Anopheles* species.

Reasons: Mosquito eggs and larva are used in the study. No animals or animal products are used in the study.

Conditions: All approved biosafety and biosecurity SOPs should be adhered to.

Should you require any further information, do not hesitate to contact me.

Yours sincerely,

Kennedy Erlwanger

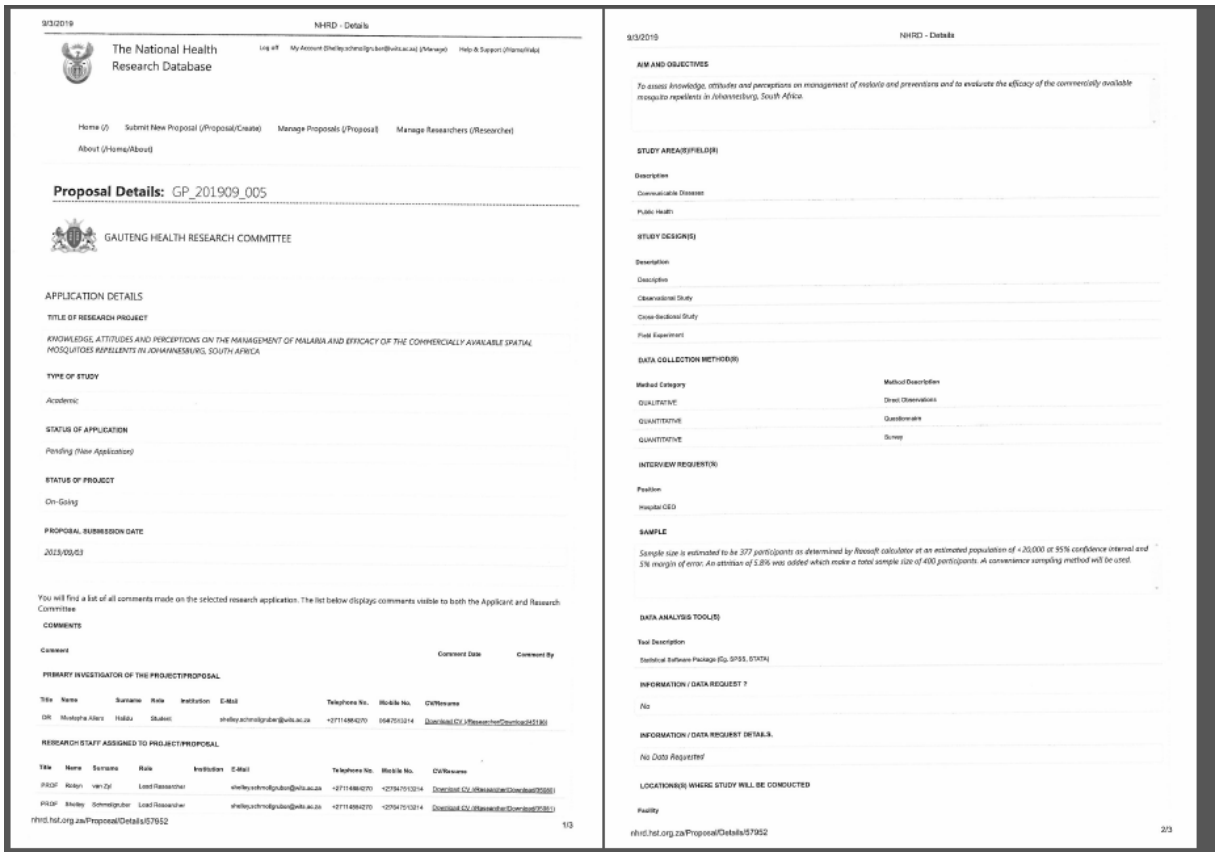
(Chairman: Animal Research Ethics Committee, University of the Witwatersrand)

Reference: R van Zyl –Anopheles Waiver 07-11-2017-O

Assoc Prof Kennedy H. Erlwanger
School of Physiology
Faculty of Health Sciences, University of the Witwatersrand
7 York Road, Parktown, 2193
SOUTH AFRICA
Tel: +27 (0)11 717 2454
Email: Kennedy.Erlwanger@wits.ac.za

APPENDIX Y

Gauteng Health Research Committee Approval



9/3/2019 NHRD - Details

The National Health Research Database

Log off My Account (Shelley.schmollgruber@wits.ac.za) (/Manage) Help & Support (/Home/Help)

Home (/) Submit New Proposal (/Proposal/Create) Manage Proposals (/Proposal) Manage Researchers (/Researcher)

About (/Home/About)

Proposal Details: GP_201909_005

GAUTENG HEALTH RESEARCH COMMITTEE

APPLICATION DETAILS

TITLE OF RESEARCH PROJECT

KNOWLEDGE, ATTITUDES AND PERCEPTIONS ON THE MANAGEMENT OF MALARIA AND EFFICACY OF THE COMMERCIALLY AVAILABLE SPATIAL MOSQUITOES REPELLENTS IN JOHANNESBURG, SOUTH AFRICA

TYPE OF STUDY

Academic

STATUS OF APPLICATION

Pending (New Application)

STATUS OF PROJECT

On-Going

PROPOSAL SUBMISSION DATE

2019/09/03

You will find a list of all comments made on the selected research application. The list below displays comments visible to both the Applicant and Research Committee

COMMENTS

Comment Comment Date Comment By

PRIMARY INVESTIGATOR OF THE PROJECT/PROPOSAL

Title	Name	Surname	Role	Institution	E-Mail	Telephone No.	Mobile No.	CV/Resume
DR	Mustapha Allen	Haliru	Student		shelley.schmollgruber@wits.ac.za	+27114864270	0647553214	Download CV (/Researcher/Download/45186)

RESEARCH STAFF ASSIGNED TO PROJECT/PROPOSAL

Title	Name	Surname	Role	Institution	E-Mail	Telephone No.	Mobile No.	CV/Resume
PROF	Robyn	van Zyl	Lead Researcher		shelley.schmollgruber@wits.ac.za	+27114864270	+27647553214	Download CV (/Researcher/Download/45186)
PROF	Shelley	Schmollgruber	Lead Researcher		shelley.schmollgruber@wits.ac.za	+27114864270	+27647553214	Download CV (/Researcher/Download/45186)

nhrd.hst.org.za/Proposal/Details/57952 1/3

9/3/2019 NHRD - Details

AIM AND OBJECTIVES

To assess knowledge, attitudes and perceptions on management of malaria and preventions and to evaluate the efficacy of the commercially available mosquito repellents in Johannesburg, South Africa.

STUDY AREA(S)/FIELD(S)

Description

Communicable Diseases

Public Health

STUDY DESIGN(S)

Description

Descriptive

Observational Study

Cross-Sectional Study

Field Experiment

DATA COLLECTION METHOD(S)

Method Category	Method Description
QUALITATIVE	Direct Observations
QUANTITATIVE	Questionnaire
QUANTITATIVE	Survey

INTERVIEW REQUEST(S)

Position

Hospital CEO

SAMPLE

Sample size is estimated to be 377 participants as determined by Raosoft calculator at an estimated population of +-20,000 at 95% confidence interval and 5% margin of error. An attrition of 5.8% was added which make a total sample size of 400 participants. A convenience sampling method will be used.

DATA ANALYSIS TOOL(S)

Tool Description

Statistical Software Package (Eg. SPSS, STATA)

INFORMATION / DATA REQUEST ?

No

INFORMATION / DATA REQUEST DETAILS.

No Data Requested

LOCATION(S) WHERE STUDY WILL BE CONDUCTED

Facility

nhrd.hst.org.za/Proposal/Details/57952 2/3

--- Charlotte Maxeke Hospital

--- Chris Hani Baragwanath Hospital

--- Helen Joseph Hospital

--- Sizwe Tropical Diseases Hospital

ANTICIPATED START DATE

2019/10/03

ANTICIPATED COMPLETION DATE

2020/03/10

INSTITUTION(S) WHICH GAVE ETHICAL APPROVAL

Institution

Wits - Human Research Ethics Committee(Medical), University Of The Witwatersrand

ETHICS APPROVAL NUMBER

M190657

DATE OF ETHICAL APPROVAL

2019/08/08

DATE ETHICAL APPROVAL EXPIRES

2020/08/08

IF CLINICAL TRIAL, MCC APPROVED

No

NATIONAL CLINICAL TRIALS REGISTRY NUMBER

No Clinical Trial

FUNDING SOURCE

Researcher

BUDGET (IN ZAR)

1 000 - 20 000

Back to List (Proposal)